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American Journal of Diseases of Children

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JULY, 1914

NO. 1

STUDIES IN THE RESPIRATORY EXCHANGE OF INFANTS *

FRANCIS G. BENEDICT AND FRITZ B. TALBOT

BOSTON

An extensive study of the gaseous exchange of infants has been in progress for three years in connection with the Nutrition Laboratory and with the Massachusetts General Hospital. Pending the development of a method for determining the oxygen consumption directly—a factor that we deemed of very great importance—a preliminary communication was made in this journal¹ in 1912. Since the appearance of this article, the apparatus and technic have been perfected so as to include direct determinations of the oxygen consumption. An apparatus has been constructed, tested and installed in a special room in the Massachusetts General Hospital, and except during the summer months, studies of the gaseous metabolism of infants have been made daily since January, 1913. Although the investigation is still in progress, sufficient data have been accumulated to justify the presentation of material *in extenso* in a publication of the Carnegie Institution of Washington.² A full description of the apparatus and technic, the clinical history of the infants studied and the statistical data for each observation are given in that publication for permanent record. It is our purpose in this communication to present first, a complete collection of the literature bearing on this subject up to the present date, and second, an amplification of our data by a new series of observations and finally an abstract of our results.

PREVIOUS OBSERVATIONS ON THE GASEOUS METABOLISM OF INFANTS

The earliest record that we have been able to find of the measurement of the gaseous metabolism of an infant is that reported by J. Forster of Munich, in 1877.[†] In an effort to explain the well-known

* Submitted for publication, May 8, 1914.

* From the Nutrition Laboratory of the Carnegie Institution of Washington and the Children's Department of the Massachusetts General Hospital, Boston, Mass.

1. Benedict and Talbot: Some Fundamental Principles in Studying Infant Metabolism, *AM. JOUR. DIS. CHILD.*, 1912, iv, 129.

2. Benedict and Talbot: The Gaseous Metabolism of Infants with Special Reference to Its Relation to Pulse-Rate and Muscular Activity, Carnegie Institution of Washington, Publication 201, 1914.

† Forster: *Amtl. Ber. d. 50. Versamml. deutsch. Naturf. u. Aerzte in München, Munich, 1877*, p. 355.

fact that children consume a larger amount of food in proportion to their body-weight than do adults, this investigator made determinations of the carbon dioxid excretion in fourteen experiments on children varying in age from 14 days to 9 years. His results all showed that 10 or 12 gm. of carbon dioxid were given off per hour for every 10 kg. of body-weight. With adults on the same basis, the carbon dioxid given off under conditions of rest and approximate hunger was 4 to 5 gm. per hour; with an average diet, 5 to 6 gm.; and with food and work, 7 gm. The author points out that the youthful organism, even in the condition of hunger, produces per unit of weight at least twice the amount of carbon dioxid which is produced by the adult body. The fact is also recognized that the infant can develop a considerable amount of work.

The experiments were made with the large Pettenkofer-Voit respiration chamber in Munich, but the protocols were never published, and aside from the statement that the children were at rest, no further details are given as to the muscular activity or the pulse-rate.

In 1885 Richet,³ in describing his calorimeter, states that he has two chambers, one of which, having a capacity of about 1,500 liters of air, is used for experiments with infants. He cites an experiment with an infant of 9 kg., who was in the chamber for one hour and ten minutes, and gives protocols for another experiment, one hour in length, presumably with the same infant. In summing up his averages he refers to numerous experiments on infants weighing from 6 to 9 kg., and includes observations made with environmental temperatures ranging from 18 C. to 25 C. He concludes that the infant produces on the average 4 calories per kilogram of body-weight per hour. Richet discusses especially the relationship between the body-surface and the heat-production.

Two years later, Langlois⁴ conducted experiments on children with Richet's calorimeter, in which only the heat-production was measured. From 17 controlled experiments, all with infants weighing about 7 kg., Langlois concludes that the heat-production is increased as the environmental temperature is lowered. As a result of a study of the influence of the time of day on the heat-production, he also concludes that there are two maximum values at approximately 11 a. m. and 3 p. m., corresponding to the values for the absorption of oxygen found by Fredericq.⁵

Langlois' discussion of the relationships between the heat-production and the body-weight and the heat-production and the body-surface

3. Richet: *Archiv. de physiol. norm. et. path.*, 1885, Series 3, xv, 237.

4. Langlois: *Centralbl. f. Physiol.*, 1887, i, 237.

5. Fredericq: *Arch. de Biol.*, 1882, iii, 731.

is of special interest in connection with our research. As will be seen from his figures given in Table 1, the smaller the child the larger was the heat-production per kilogram of body-weight. The author points out, however, that if the heat-production and body-surface are compared, as is done in Table 2, the uniformity is remarkable. He gives a very unsatisfactory explanation of his unit of surface, but brings out the fundamental idea that the heat per unit of body-surface is essentially the same for an infant as for an adult weighing 65 kg., namely, 14 to 17 calories. No information is given regarding the muscular activity, the age, or the pulse-rate of these infants.

In another paper, Langlois⁶ refers to Richet's observations on normal children weighing from 7 to 10 kg. with a heat-production of approximately 4,000 calories per kilogram per hour, and reports his own results with sick infants in which he finds a direct relationship

TABLE 1.—RELATIONSHIP BETWEEN HEAT-PRODUCTION AND BODY-WEIGHT OF INFANTS (LANGLOIS)

Body-Weight (kg.)	Heat-Production per kg. of Body-Weight (cals.)
Two children1.8	6.40
Child2.5	4.80
Children from.....3.0 to 4.0	4.20
Children from.....7.0 to 8.0	4.12
Children from.....9.0 to 10.0	3.93

between body-temperature and heat-production. Infants having temperatures below 37.5 C., which he takes as normal, had a heat-production less than 4 calories per kilogram of body-weight per hour, while those with temperatures above 37.5 C. had a higher heat-production; thus, with a body-temperature of 35.5 C., the heat-production was equal to 2,900 calories, while with a body-temperature of 40.5 C., it was equal to 4,600 calories.

Langlois' calorimeter was subsequently used by Variot and Saint-Albin⁷ in studying the calorimetry of atrophic infants. The tests of this calorimeter published by Saint-Albin⁸ show a possible error of plus or minus 10 per cent., thus indicating that the apparatus can hardly be

6. Langlois: *Compt. rend de l'Acad. des Sci. de l'Institut de France*, 1887, civ, 860.

7. Variot and Saint-Albin: *Bull. Soc. de pédiat.*, 1903, v, 246 and 307. See, also, an extensive discussion of these researches in the thesis by Saint-Albin: *Etude sur la calorimétrie des infants atrophiques*, Paris, 1904, No. 295.

8. Saint-Albin: *Etude sur la calorimétrie* (Note 7), p. 25.

considered an instrument of precision. As Saint-Albin points out himself, his check tests differ considerably from those of Langlois.

Variot and Saint-Albin studied a large number of atrophic infants. Their conclusions, reported by Saint-Albin, are especially interesting in connection with this report of our researches, since they show that (using their terminology) out of 33 atrophic infants, there were 11 "*hyperrayonnants*," 16 "*hyporayonnants*" and 6 "*rayonnants normalement*."⁹

Of the numerous forms of calorimeters reported to the French scientific societies by d'Arsonval, one¹⁰ was employed by Bonniot¹¹ in 1898 for a study of the heat-production of infants with temperature disturbances, but he found no regular relationship between heat radia-

TABLE 2.—RELATIONSHIP BETWEEN HEAT PRODUCTION AND BODY-SURFACE OF INFANTS (LANGLOIS)

Body-Weight kg.	Body-Surface	Heat-Production		
		Per kg. of Body-Weight Cals.	Per Unit of Surface cals.	Per Sq. Meter of Body-Surface† cals.
10	9.142*	3.920	17	1,690
9	2.106	3.900	16	1,620
7	1.778	4.120	16	1,580
6	1.638	4.200	15	1,500
4	1.135	4.300	15	1,370
2	0.780	6.000	15	1,510

* This figure is quoted from Langlois and as his discussion of body-surface is very confusing, it is impossible to make a correction, which is obviously much needed.

† As calculated by Camerer using Meeh's formula (Camerer: *Der Stoffwechsels des Kindes*, Tübingen, 1896, p. 109).

tion and rectal temperature. A detailed presentation of Bonniot's results may be found in his thesis.¹²

The most recent contribution from French laboratories on direct calorimetry with which we are familiar is that of Variot and Lavalie¹³ in 1912. In this interesting communication, in which the fundamental principles of infant calorimetry are well considered, the authors state

9. Saint-Albin: *Etude sur la calorimétrie* (Note 7), p. 39.

10. See note on this particular calorimeter by d'Arsonval: *Mem. Soc. de biol.*, 1898, p. 248.

11. Bonniot: *Mém. Soc. de biol.*, 1898, p. 249. For a critique of the Richet and d'Arsonval calorimeters, see Bonniot: *Calorimétrie infantile état de la question*, *Clinique Infantile*, 1906, iv, 289.

12. Bonniot: *De l'hyperthermie dans la fièvre; essai de calorimétrie clinique*, Paris, 1900, No. 419.

that they used the modified form of the d'Arsonval calorimeter which was calibrated by electrical resistance. The gaseous metabolism was not studied and no statement was made as to the muscular activity of the infants. The authors conclude that the heat-output of infants increases in proportion as the weight decreases and lay great emphasis on the effect of clothing on radiation. They likewise believe that the supply of adipose tissue may materially modify the radiation.

Mensi¹⁴ of Turin, without stating the apparatus employed or even the fundamental principle, reports a series of observations on five newborn infants varying in age from 6 hours and 5 minutes to 7 days, 17 hours and 54 minutes. In these experiments the oxygen consumption was determined as well as the carbon dioxid production. The results are given in Table 3. The statement is made that the infants were quiet in each case, but no pulse records are given.

A very interesting series of experiments on infants was carried out by Scherer in the institute of Professor Marès in Prague¹⁵ with an apparatus on the Regnault-Reiset principle, the oxygen being supplied from a bomb. The author states that the infants found themselves in "complete physiological condition" inside the chamber. In this series, fifty-five experiments were made in the spring and summer and thirty experiments in the winter, each one being about two hours long. No information is given regarding the activity of the infants or the pulse-rate. The fact that the average respiratory quotients were considerably below 0.6 points strongly to an error in the method. The author concludes that the intensity of the respiratory exchange is dependent on the body-weight and is inversely proportional to it.

Two years later the classic monograph of Rubner and Heubner¹⁶ appeared. In discussing the earlier observations of Forster, they add the significant fact that Forster's experimental periods were but one hour long. As their own work was done with the Pettenkofer chamber, they criticize adversely the closed circuit apparatus used by Scherer, and particularly the fundamental principle of using experiments with short periods, their paper setting forth fully the arguments in favor of the long experimental period and the Pettenkofer type of respiration chamber as compared with the short period and the Regnault-Reiset chamber. The Pettenkofer chamber, which had pre-

13. Variot and Lavialle: Bull. and mém. Soc. méd. d. hôp. de Paris, 1912, Series 3, xxxiii, 410. See, also, Clinique Infantile, 1912, x, 229, and Report of the Congrès National des Gouttes de Lait tenu à Fécamp les 26, 27, et 28 Mai, 1912, p. 79.

14. Mensi: Gior. d. r. Accad. di med. di Torino, 1894, lvii, 301.

15. Scherer: Jahrb. f. Kinderh., 1896, new series, xliii, 471.

16. Rubner and Heubner: Ztschr. f. Biol., 1898, xxxvi, 1.

TABLE 3.—SUMMARY OF EXPERIMENTS ON RESPIRATORY EXCHANGE OF NEW-BORN INFANTS
(MENSI)

Age d., h., m.	Sex	Body- Weight kg.	Length of Experi- ment minutes	Oxygen Consumed			Carbon Dioxid Produced			Respir- atory Quo- tient	
				Total c.c.	Per Minute c.c.	Per Kg. per Min. c.c.	Total c.c.	Per Min. c.c.	Per Kg. per Minute		
									c.c.		mg.
6 5	M.	2.70	173	5,707	32.9	12.18	4,174	24.1	8.92	16.08	0.73
1 2 47	M.	3.00	173	6,470	37.4	12.46	3,844	22.2	7.40	13.34	0.593
3 1 55	M.	2.92	159	6,216	39.09	13.38	3,442	21.64	7.41	13.36	0.55
3 7 22	F.	2.47	171	5,463	31.9	12.91	3,586	20.9	8.46	15.25	0.655
7 17 54	M.	2.32	149	4,997	33.5	14.43	2,979	19.9	8.57	15.45	0.59

viously been described,¹⁷ was slightly modified for the studies of Rubner and Heubner, a small chamber being used.

The fundamental question studied by Rubner and Heubner was the nourishment of an infant from a practical point of view; and they were accordingly more interested in the average daily requirement of an infant for nourishment than in the physiologic fact of the minimum requirement for comparison with other individuals. The subject—a “normal” infant—was 9 weeks old at the time of the observation and weighed 5,220 gm. The infant was placed in the respiration chamber and removed and fed from six to eight times each day, the time thus lost being carefully recorded. Ocular observations of the muscular activity were made and a general impression for each day recorded. For much of the time, the infant was awake but not crying. On the basis of twenty-four hours the authors found a difference of 22 per cent. between the minimum and maximum carbon dioxid production. They state that this difference is due to the unequal activity of the infant, emphasizing especially the fact that disturbance of sleep during the night influences the total daily average of the metabolism.

Using the formula of Meeh¹⁸ and a body-weight of 5.1 kg., they compute the body-surface to be equal to 3,500 square centimeters and find a carbon dioxid production of 13.5 gm. per square meter of body-surface per hour. Comparing this value with those values found with adults, they state that the infant excreted less carbon dioxid per square meter of body-surface than did the adults, and explain this by the fact that the infant was asleep a part of the time while the determinations with adults were made only when the subjects were awake. Having pointed out that their results contradict those of Sondén and Tigerstedt,¹⁹ which showed an increased production of carbon dioxid in youth, they emphasize the fact that the carbon dioxid is essentially proportional to the body-surface with human individuals of any size.

Shortly after the publication of their investigations with a normal, breast-fed infant, Rubner and Heubner²⁰ reported a comparative study with a normal and an atrophic infant, neither being breast-fed. This study was carried out on the same plan as that used for the former experiment. The “normal” infant weighed 7.57 kg., was 7½ months old and appeared to be in good health. She was fed on milk and milk-sugar and throughout the observation was said to be in general *recht ruhig*. The results were compared with those obtained with the breast-fed infant in the previous experiment, the hourly excretion of carbon

17. Wolpert: Arch. f. Hyg., 1896, xxvi, 32.

18. Meeh uses the formula $S = 11.9 \sqrt[3]{\frac{W}{a}}$. (Ztschr. f. Biol., 1879, xv, 425.)

19. Sondén and Tigerstedt: Skandin. Arch. f. Physiol., 1895, vi, 1.

20. Rubner and Heubner: Ztschr. f. Biol., 1899, xxxviii, 315.

dioxid per square meter of body-surface being but 13.5 gm. for the breast-fed infant, which weighed but 5 kg., and 17.3 gm. for the artificially fed infant, which weighed 7.6 kg.

The second portion of the paper deals with the metabolism of the atrophic infant, artificially fed with cow's milk and "*Kindermehl*." Their results are given in Table 4. The authors conclude that there was nothing abnormal in the metabolism of the atrophic infant.

The first extensive study exclusively with atrophic infants was made by Poppi.²¹ A respiration apparatus of the closed-circuit type was probably used, as both the carbon dioxid production and the oxygen consumption were measured, though little is said of the method. An abstract of the results obtained with seven infants is given in Table 5. The respiratory quotients all seem unusually high, and this fact throws doubt on the accuracy of the research. It is probable,

TABLE 4.—RESULTS OF EXPERIMENTS WITH A NORMAL INFANT AND AN ATROPHIC INFANT. (RUBNER AND HEUBNER)

Description of Subject	Food	Period	Calories per Square Meter of Body-Surface
Normal.....	Breast-fed	1,006
	Cow's milk.....	I	1,143
	Cow's milk.....	II	1,233
	Cow's milk.....	III	1,378
Atrophic.....	Cow's milk.....	I	1,090
	Cow's milk.....	II	1,171
	Meal	1,036

however, that the carbon dioxid determinations are well within the limits of accuracy, as is usual with methods of this type. From the protocols of one of Poppi's studies, it appears that the experiments were each two hours long, but no estimations are given regarding the muscular activity or the pulse-rate.

In 1904 Rubner and Heubner²² reported another series of experiments covering a period of five days. The subject was a breast-fed infant, 5½ months old and weighing 9.7 kg. Notwithstanding the apparently large changes in the activity from day to day, the investigators found that the carbon dioxid output on the last four days was fairly constant—a fact which puzzled the authors, who suggest a compensatory influence in the life of the infant. They compare the results found in this observation with those secured with other infants

21. Poppi: Il ricambio materiale e il ricambio respiratorio nell'atrofia infantile, Bologna, 1900.

22. Rubner and Heubner: Ztschr. f. exper. Path. u. Therap., 1904-05, i, 1.

TABLE 5.—RESULTS OF EXPERIMENTS ON THE RESPIRATORY EXCHANGE OF ATROPHIC INFANTS (Poppi)

Name	Date 1899	Dura- tion hrs., min.	Body- Weight kg.	Age mos.	Carbon Dioxid Produced			Oxygen Consumed			Respir- atory Quo- tient
					Total c.c.	Per 24 Hours liters	Per Kg. per Min c.c.	Total c.c.	Per 24 Hours liters	Per Kg. per Min c.c.	
P. L.....	July 11	1 15	3.425	9	2,166	40.62	8.237	2,084	40.02	8.114	1.015
N. B.....	July 20	2 00	3.865	10	3,900	46.80	8.409	3,820	45.84	8.236	1.021
C. F.....	Nov. 10	2 00	5,500	16	4,125	49.50	6.25	4,621	55.452	7.002	0.893
A. F.....	Nov. 12	2 00	3.465	7	3,177	38.13	7.642	3,027	36.324	7.280	1.050
M. G.....	Nov. 15	2 00	5.450	12	4,071	48.852	6.225	4,186	50.232	6.40	0.973
F. G.....	Dec. 8 1900	2 00	2.780	3½	2,667	32.004	8.07	2,642	31.704	7.92	1.019
E. N.....	Feb. 3	2 00	3.940	4	3,009	36.108	6.364	3,223	38.676	6.818	0.933

in the previous work done by them, and find an increase in the carbon dioxid output of 21 per cent. over the results obtained with the breast-fed infant previously studied. (See Table 6.) This increase they explain by saying that it is due to the greater activity of the infant in the last experiment.

TABLE 6.—METABOLISM OF INFANTS COMPARED (RUBNER AND HEUBNER)

Subjects and Diet	Body-Weight, kg.	Calories per Square Meter of Body-Surface per Day
Atrophic child (cow's milk)	3	1,090
Breast child	5	1,006
Child (cow's milk)	8	1,143
Child (breast. of this experiment)	10	1,219

In 1908 a report appeared of the first in a remarkable series of experiments carried out by Schlossmann and Murschhauser in Düsseldorf.²³ The protocols of this experiment were given in connection with a description of the testing of the modified Regnault-Reiset apparatus constructed by Zuntz and Oppenheimer. The authors, Schlossmann, Oppenheimer and Murschhauser, emphasize the importance of observa-

TABLE 7.—METABOLISM OF AN INFANT (SCHLOSSMANN AND MURSCHHAUSER)
(PER SQUARE METER OF BODY-SURFACE PER HOUR)

	Oxygen Consumption, gm.	Carbon-Dioxid Production, gm.
Average during eight hours' sleep	11.0	13.78
Shortly after feeding....	11.88	15.52
Three hours after feeding	10.42	12.68
Waking and sleeping....	12.85	15.75

tions when the infant is asleep; they accordingly preferred to make their observations the first half of the night, feeding the infant with a large amount of breast-milk in the early evening. The measurements of the metabolism of the infant during this experiment are given in Table 7. During the experimental period the infant weighed 5.79 kg., the calculated body-surface²⁴ being 0.384 square meters.

23. Schlossmann, Oppenheimer and Murschhauser: *Biochem. Ztschr.*, 1908, xiv, 385.

24. Surface = $11.9 \sqrt{\frac{W}{72}}$

The same infant was subsequently studied by Schlossmann and Murschhauser²⁵ at the ages of 144 days, 284 days and 380 days. They found no difference in the metabolism per square meter of body-surface and conclude that Rubner's law is correct and that the metabolic processes are proportional to the body-surface.

The report of the first extensive research made by Schlossmann and Murschhauser appeared in 1910.²⁶ This is of special interest, inasmuch as the authors recognize at the outset the importance of muscular repose and of determining the basal metabolism. Many valuable suggestions as to the selection of infants for such study are incorporated in the report. Observations were made on three female infants; the results of these are given in Table 8. The authors conclude that the carbon dioxid production and the oxygen consumption depend on the body-surface, being wholly independent of the age of

TABLE 8.—RESULTS OF FASTING EXPERIMENTS WITH INFANTS DURING APPROXIMATELY ABSOLUTE REST. (SCHLOSSMANN AND MURSCHHAUSER)

Subject	Age Days	Weight kg.	Body-Surface Square Meter	Carbon Dioxid per Square Meter per Hour, gm.	Oxygen per Square Meter per Hour gm.	Respiratory Quotient
S.....	174	5.010	0.3505	12.27	10.56	0.847
	180	5.115	0.3553	12.22	10.81	0.824
P.....	149	4.220	0.3124	12.35	10.52	0.856
	169	4.430	0.3228	12.64	11.08	0.832
L.....	87	4.980	0.3491	12.33	12.22	0.730
	93	5.040	0.3519	11.48	10.93	0.760

the subject, and draw the general conclusion that the infant produces per square meter of body-surface about 12 gm. of carbon dioxid and consumes about 11 gm. of oxygen per hour.

Recognizing the possibility that the environmental temperature may have an effect on the metabolism of the infant, Schlossmann and Murschhauser discussed this point in 1911,²⁷ giving the results of experiments with an infant in which the temperature of the surrounding atmosphere varied from 16.3 C. to 23.4 C. Another infant was studied with temperatures varying from 16.9 C. to 23.4 C. The results of this second experiment substantiated those obtained with the first infant, and the authors feel justified in concluding that the slight temperature changes found in experiments with an apparatus of the

25. Schlossmann and Murschhauser: *Biochem. Ztschr.*, 1909, xviii, 499.

26. Schlossmann and Murschhauser: *Biochem. Ztschr.*, 1910, xxvi, 14.

27. Schlossmann and Murschhauser: *Biochem. Ztschr.*, 1911, xxxvii, 1.

Regnault-Reiset type are entirely without influence on the metabolism of the individuals studied.

The same investigators,²⁸ with a keen appreciation of the influence of muscular activity on metabolism, compared the results of observations with an infant who cried continuously for an hour with those obtained when the infant was approximately quiet. They estimated that the crying increased the carbon dioxid production 59.4 per cent. and the oxygen consumption 44 per cent.

In still another paper Schlossmann²⁹ discusses the general principles involved in the measurement of the respiratory exchange of infants and emphasizes the necessity of muscular repose and the absence of food, and the importance of measuring the basal metabolism. He again asserts that the heat per square meter of body-surface is constant and maintains that this is a proof that the metabolism of young individuals is not variable. In this paper, also, he discusses the amount of work the infant does, basing the discussion on results obtained in his experiments with crying infants. In many of his experiments Schlossmann measured the skin temperature of the infant by electrical methods and found that there was no increase in the temperature.

In a paper discussing his earlier experiments on infants of varying ages and particularly those with an atrophic infant, Schlossmann opposes the views defended by Kassowitz,³⁰ that the metabolism in smaller animals is more intense than in the large animals and that there is no relationship between the metabolism and the body-surface.³¹ Schlossmann maintains that atrophic infants have a higher metabolism per unit of body-surface than normal infants, but that this points to the correctness of the Rubner law, since with these infants the relation between body-surface and body-weight is abnormal. As he made no measurements of the body-surface of these infants — a procedure that necessitated an enormous amount of work — no direct evidence is offered to show that there was an actual disproportion between the body-surface and the body weight.

In a paper which appeared after the publication of Schlossmann's criticism, Kassowitz³² sums up his arguments against the belief that the metabolism is proportional to the body-surface, and using Schlossmann's own protocols, criticizes adversely the latter's deductions.

In a paper which has only recently appeared³³ Schlossmann again discusses the degree of activity and the amount of work done by

28. Schlossmann and Murschhauser: *Biochem. Ztschr.*, 1911, xxxvii, 23.

29. Schlossmann: *Deutsch. med. Wchnschr.*, 1911, xxxvii, 1633.

30. Kassowitz: *Allgemeine Biologie*, Vienna, 1904, iii, 221.

31. Schlossmann: *Ztschr. f. Kinderh.*, 1912-13, v, 227.

32. Kassowitz: *Ztschr. f. Kinderh.*, 1913, vi, 240.

33. Schlossmann: *Monatschr. f. Kinderh.*, 1913, xii, 47. See also *AM. JOUR. DIS. CHILD.*, 1913, vi, 15.

infants in crying. He strongly emphasizes the necessity of noting the degree of repose during the observation, either by the ocular method used by himself or the graphic record devised in this laboratory. Unfortunately, at the time this paper was written, Schlossmann had not been able to compare the two methods.

Two later communications by Schlossmann and Murschhauser³⁴ on the metabolism of fasting infants have particular significance in connection with this report, as they discuss the ideal conditions for obtaining the basal metabolism.

Using a Pettenkofer-Voit respiration apparatus³⁵ in the Kaiserin Auguste Victoria-Haus in Charlottenburg, Birk and Edelstein³⁶ studied the respiratory exchange of a healthy, new-born infant weighing 3.2 kg. and having a length of 50 cm. The infant was completely wound in cotton wool so as to keep the body-temperature at a normal level. Although he was removed from the respiration chamber several times during the day, the infant remained in the apparatus for the greater part of the twenty-four hours. On the second day the carbon dioxid production per twenty-four hours was 55.6 gm., or 18.2 gm. per kilogram; on the third day the total amount was 47.59 gm., or 15.76 gm. per kilogram per twenty-four hours. The authors criticize the use of short experiments with a respiration apparatus by which the oxygen consumption can be determined and the respiratory quotients calculated, but express regret that with their method the oxygen consumption cannot be determined.

In a study made by Carpenter and Murlin³⁷ of the energy metabolism of pregnant women before and after the birth of the child, the energy metabolism of three new-born infants was also found per unit of weight and per unit of body-surface. The values were obtained by subtracting the measured metabolism of the mother from that of the mother and infant together.

The metabolism of an atrophic infant was studied by Niemann,³⁸ who used a Pettenkofer-Voit respiration apparatus in the children's clinic of the University of Berlin. The observation continued six days, the infant remaining in the chamber the greater part of each day. The measurements of the carbon dioxid production on the basis of twenty-four hours are given in Table 9. When these results are computed on the basis of carbon dioxid produced per square meter of body-surface,

34. Schlossmann and Murschhauser: *Biochem. Ztschr.*, 1913, lvi, 355; *ibid.*, 1914, lviii, 483.

35. Bahrdt and Edelstein: *Jahrb. f. Kinderh.*, 1910, lxxii, 43.

36. Birk and Edelstein: *Monatschr. f. Kinderh.*, 1910, ix, 505.

37. Carpenter, T. M., and Murlin, J. R.: *The Energy Metabolism of Mother and Child Just Before and Just After Birth*, *Arch. Int. Med.*, 1911, vii, 184.

38. Niemann: *Ztschr. f. Kinderh.*, 1913, vi, 375.

using the formula of Meeh and the constant 11.9, the author finds that this infant with an average body-weight during the six days of 3.28 kg. had a body-surface corresponding to 0.2626 square meter, and that the carbon dioxid excretion per square meter of body-surface was 18.5 gm. per hour.

TABLE 9.—RESULTS OF AN EXPERIMENT WITH AN ATROPHIC INFANT (NIEMANN)

Day	Carbon-Dioxid Production per Day gm.	Average Temperature of the Air, °C.
1	108.0	20.5
2	110.4	20.0
3	117.6	21.0
4	115.2	21.0
5	120.0	21.0
6	127.2	21.0
Maximum..	127.2	
Minimum..	108.0	
Average....	116.4	

The metabolism of another atrophic infant was studied in the Universitäts-Kinderklinik, Berlin, by Frank and Wolff.³⁹ Using the Pettenkofer-Voit respiration apparatus modified by Rubner, they made two series of experiments of four days each. The average values for carbon dioxid are given in Table 10. The authors especially comment

TABLE 10.—AVERAGE CARBON-DIOXID EXCRETION IN EXPERIMENTS WITH AN ATROPHIC INFANT (FRANK AND WOLFF)

	Period I	Period II
Total twenty-four hours.	127.61	148.81
Per hour	5.317	6.151
Per kilo per twenty-four hours	34.44	38.95
Per kilo per hour.....	1.435	1.623
Per square meter per hour876	21.26

on the unusually high figures for the carbon dioxid excretion, and attempt to explain them by the disturbance between the computed body-surface and body-weight and the effect of a protein-rich diet, but expressly maintain that muscular activity played no rôle as the infant, except on the first day, was *sehr ruhig*.

39. Frank and Wolff: Jahrb. f. Kinderh., 1913, lxxviii, 1.

Bahrdt and Edelstein⁴⁰ also report an experiment with an atrophic infant, in which they used the respiration apparatus in Langstein's laboratory in the Kaiserin Auguste Victoria-Haus. The observation was made in three periods of four days each. In the first and last periods, the infant remained inside the chamber for the greater part of the twenty-four hours, being removed periodically, as is customary in experiments with this type of apparatus. Their final conclusion was that the heat-production of atrophic infants can be abnormally high aside from any effect which the environmental temperature or the body activity may have on it.

Finally, the direct calorimetric and gasometric researches of Howland⁴¹ in Lusk's laboratory should be especially noted. In discussing the calculation of the body-surface, Howland cites the use of the factor 12.3 as a constant for infants, but we are not aware of any writers who have previously used this factor. The experiments were made with the respiration calorimeter⁴² at the Cornell University Medical College in New York. Three infants under 1 year of age were studied and ocular observations of the activity of the infants were recorded.

Howland's experiments were subsequently published in detail and the results more fully discussed.⁴³ In this paper the relationship between body-surface and body-weight is extensively treated and the various factors and formulas are considered. A curve is proposed, which is represented by the algebraic expression $y = mx + b$, in which y is the surface area of the infant, x the weight of the infant in grams, m the constant 0.483, and b , 730 sq. cm.

The last portion of the paper, which is of most significance, compares the direct and indirect computation of the heat-production of the infants observed. This comparison is of such value to workers in metabolism that it is given here in Table 11. The agreement between the heat-production as directly measured and as indirectly computed is striking, to say the least, and justifies for the present the utilization of the indirect method of computing the calorimetry of infants.

Though Howland, using Lusk's calorimeter, has been eminently successful in experiments on the direct calorimetry of infants, experience with such researches in the Nutrition Laboratory has led us to believe that a type of calorimeter with less mass, less heat capacity, and probably not of the continuous-flow type could most advantage-

40. Bahrdt and Edelstein: Festschrift Dr. Otto L. Heubner, 1913, Berlin.

41. Howland: Proc. Soc. Exper. Biol. and Med., 1911, viii, 63; (Hoppe-Seyler's) Ztschr. f. physiol. Chem., 1911, lxxiv, 1.

42. Williams: Jour. Biol. Chem., 1912, xii, 317.

43. Howland: Tr. Fifteenth Internat. Cong. Hyg. and Demog., 1912, ii, 438. (Pub. Washington, 1913.)

ously be employed for the short periods necessitated by experiments with infants. Several types or modifications of calorimeters have been in process of testing for some time, and pending the satisfactory development, construction and testing of an infant calorimeter with the qualifications referred to, we have actively undertaken the study of infant metabolism as determined by indirect calorimetry. In these observations we have devoted our energies to the accurate measurement, in relatively short periods, of the carbon dioxide produced and oxygen consumed by infants less than 1 year of age.

TABLE 11.—HEAT-PRODUCTION OF INFANTS, DIRECTLY AND INDIRECTLY MEASURED, AS REPORTED BY HOWLAND

Subject	Food	Calories per Sq. M. per Day		Difference per cent.
		Measured	Calculated	
Child 1.....	Ordinary	{ 1,046 1,113 1,196	{ 1,084 1,174 1,164	2
Child 1.....	Nutrose added	{ 1,218 1,204	{ 1,179 1,180	3
Child 1.....	Nutrose added	{ 1,235 1,181	{ 1,212 1,250	1—
Child 1.....	Fasting	{ 1,106 1,226 1,301	{ 1,177 1,156 1,243	1—
Child 3.....	Ordinary	{ 858 915	{ 793 933	2
	Ordinary	825	840	2

INDIRECT CALORIMETRY

A number of physiologists have used the respiratory exchange to compute the total calorimetry by the method of so-called "indirect calorimetry."⁴⁴ From analyses of the urine and from a careful study of the respiratory exchange it is possible to apportion the catabolism between protein, fat and carbohydrate according to methods worked out most carefully by Zuntz and his associates. Having apportioned this catabolism, it is relatively simple to compute the total caloric output from the well-known heat of combustion of the various nutrients. Thus, for every gram of nitrogen in the urine, it has been definitely shown that 26.51 calories are developed; for every gram of carbo-

44. This method is not to be confused with the usage of certain French writers who consider "indirect calorimetry" as indicating the computation of material consumed by noting the weights of food eaten, excreta, and gain or loss of body-weight.

hydrate burned in the body, not far from 4 calories are produced, and for every gram of fat, 9.5 calories.⁴⁵

A simpler method of computing the total heat, however, is to utilize the respiratory quotients, that is, the ratio between the carbon dioxide produced and the oxygen burned. Accordingly, if one knows exactly the respiratory quotient, the total carbon dioxide produced, and the oxygen absorbed, it is relatively simple to compute the total energy by using the so-called calorific equivalent for either carbon dioxide or oxygen. These calorific equivalents have also been most carefully studied by Zuntz and his associates, and as a result we have a very helpful table which gives the calorific equivalent of carbon dioxide with various respiratory quotients. When pure fat is burned, the respira-

TABLE 12.—CALORIFIC EQUIVALENTS OF CARBON DIOXID

Respiratory Quotient	Calorific Value of Carbon Dioxid		Respiratory Quotient	Calorific Value of Carbon Dioxid		Respiratory Quotient	Calorific Value of Carbon Dioxid	
	Per Liter cals.	Per gm. cals.		Per Liter cals.	Per gm. cals.		Per Liter cals.	Per gm. cals.
0.70	6.694	3.408	0.80	6.001	3.055	0.90	5.471	2.785
0.71	6.606	3.363	0.81	5.942	3.025	0.91	5.424	2.761
0.72	6.531	3.325	0.82	5.884	2.996	0.92	5.378	2.738
0.73	6.458	3.288	0.83	5.829	2.967	0.93	5.333	2.715
0.74	6.388	3.252	0.84	5.774	2.939	0.94	5.290	2.693
0.75	6.319	3.217	0.85	5.721	2.912	0.95	5.247	2.671
0.76	6.253	3.183	0.86	5.669	2.886	0.96	5.205	2.650
0.77	6.187	3.150	0.87	5.617	2.860	0.97	5.165	2.629
0.78	6.123	3.117	0.88	5.568	2.835	0.98	5.124	2.609
0.79	6.062	3.086	0.89	5.519	2.810	0.99	5.085	2.589
						1.00	5.047	2.569

tory quotient is not far from 0.71, and Zuntz has shown that for every liter of carbon dioxide produced by burning pure fat, 6.606 calories are liberated, or 3.363 calories per gram of carbon dioxide. On the other hand, when pure carbohydrates are burned, the ratio between carbon dioxide and oxygen is 1.00, that is, for every liter of carbon dioxide produced, 1 liter of oxygen is absorbed. Under these conditions Zuntz has shown that each liter of oxygen consumed corresponds to 5.047 calories, or 2.569 calories per gram of carbon dioxide.

An extremely simple method for calculating the catabolism, therefore, is to multiply the total amount of carbon or oxygen measured by the corresponding calorific equivalent. As a matter of fact, Zuntz in his work has used most frequently the calorific equivalent of oxygen, for in his method of studying the respiratory exchange the determina-

45. The heat of combustion of anhydrous cow's milk fat is 9.2 calories.

tions of oxygen are somewhat more exact than are those of carbon dioxid. Since, in our respiration apparatus, the carbon dioxid determinations for short periods are even more exact than are the determinations of the oxygen, we give in Table 12 the calorific equivalents of carbon dioxid with the varying respiratory quotients, particularly as this table will be used extensively in the computation of our own researches.

As any form of indirect calorimetry must of necessity be somewhat speculative,* one must always rely for fundamental values on direct heat measurements. Such measurements have been extensively made with men by Atwater and his associates at Wesleyan University, Middletown, Conn., where it was shown in experiments of long duration that the heat output as measured directly by the respiration calorimeter and the heat output as computed from the respiratory exchange agreed remarkably well. It should be pointed out, however, that these computations were based on twenty-four-hour periods. In certain experiments the computation has likewise been successful for periods as short as six hours, but it remained for Howland⁴⁶ to demonstrate with Lusk's calorimeter the complete agreement of the direct calorimetric measurements and of the computation from the gaseous exchange for short periods and particularly with an infant as subject. This being the case, the field is open for making a large number of metabolism experiments with the respiration apparatus in laboratories and institutions where a respiration calorimeter for direct calorimetry is not available.

BASAL METABOLISM

While the normal life of the infant is a relatively simple and constant one, yet it does include periods of muscular activity which vary greatly, the extremes ranging from perfect muscular repose during sleep to the violent exercise incidental to vigorous crying. As a result of these changes in muscular activity, the output of heat would likewise vary largely, with a minimum output during sleep and quiet and a maximum during the period of crying. An attempt has been made to find the average value for the heat output of an infant by

46. Howland: Tr. Fifteenth Internat. Cong. Hyg. and Demog., Washington, 1913, ii, 451.

* It will be noted that in this paper the computation of the energy derived from protein is neglected and that the total energy output is computed only from the amounts of carbon dioxid and oxygen. The possible error in neglecting the protein has been computed by Magnus Levy to be somewhat under 1 per cent., and as the determinations of nitrogen were not feasible in our studies, we have used the method of simple computation from the gaseous exchange as recommended by A. Loewy: Oppenheimer's *Handbuch der Biochemie*, Jena, 1911, iv, 281. See, also, Magnus-Levy: von Noorden's *Handbuch der Pathologie des Stoffwechsels*, Berlin, 1896, i, 207.

experiments with twenty-four-hour periods, thus securing an average for the life of the day; but when one considers that the difference between the heat output in complete muscular repose during sleep and the heat given off when the infant is crying vigorously may be as great as 60 or more per cent., it will be seen that this method of averaging does not furnish information with regard to the minimum metabolism.

The muscular activity of infants is twofold: (1) internal muscular activity, consisting of muscular tonus, the movements of the organs of circulation and respiration, and possibly the processes of digestion; and (2) external muscular activity such as the movements of the limbs or vigorous body movement incidental to crying. The internal movements can be controlled only by minimizing the after-effects of digestion through the absence of food; the regular involuntary muscular activity of the respiratory and circulatory system and the muscular tonus cannot be altered. On the other hand, the external muscular activities are at a minimum only during complete muscular repose, as in deep sleep. It is thus seen that the ideal conditions for studying the basal or minimum metabolism of infants would be the postabsorptive state, that is, sufficiently long after the last meal to insure that there was no longer an absorption of food materials from the alimentary tract, and during deep sleep when there is complete muscular repose. With very young infants, periods of complete muscular repose cannot be expected for any great length of time, probably not for more than two successive hours.

We have, then, two factors to deal with: first, the heat elimination incidental to the specific catabolic stimuli of the food materials accompanying the digestion and absorption of food, and second, the internal muscular activity of the infant. If the first of these factors can be eliminated, we have what may properly be termed the basal metabolism unaccompanied by extraneous muscular activity of any kind.

Accordingly, in our first years of experimenting, we have based our study of the metabolism of infants on the careful determination of the carbon dioxid production and oxygen consumption of infants under one year in a special form of respiration apparatus, under conditions favoring the accumulation of accurate information regarding the basal metabolism.

RESPIRATION APPARATUS

The apparatus used in this research was a modified form of that briefly described by us in our first communication.⁴⁷ The essential modifications are, first, arrangements for continuous observations

47. Benedict, F. G., and Talbot, F. B.: Some Fundamental Principles in Studying Infant Metabolism, *AM. JOUR. CHILD. DIS.*, 1912, iv, 130.

whereby periods of any desired length can be secured, and, second and most important, the method of determining the oxygen consumption directly. The apparatus has been carefully controlled by burning known weights of alcohol, securing not only the respiratory quotients, but likewise the total amount of carbon dioxid and oxygen corresponding to the given amount of alcohol burned. For a complete description of this apparatus and tests made with it, reference may be made to the large publication previously referred to.⁴⁸ As the infant gives off carbon dioxid and consumes oxygen, the air leaving the chamber is rich in carbon dioxid and water-vapor from the lungs and skin of the

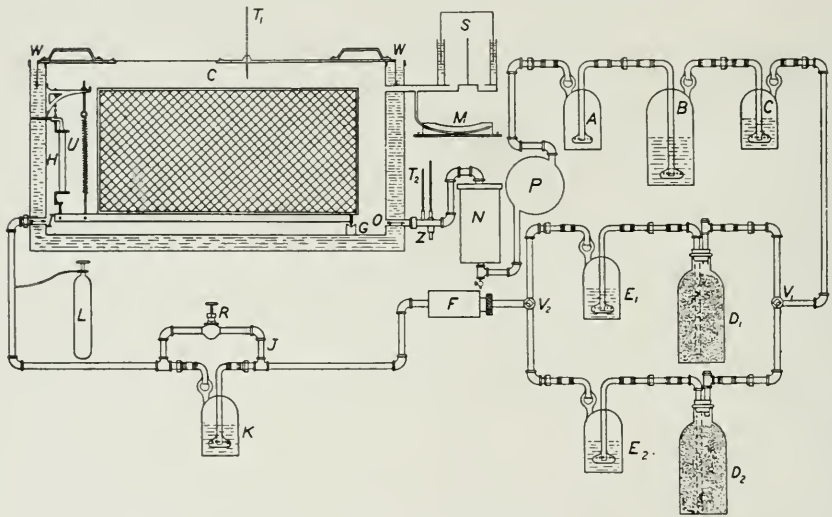


Fig. 1.—Detailed scheme of respiration apparatus. *C*, chamber; *W*, *W*, water jacket; *O*, outgoing air-pipe; *Z*, psychrometer; *N*, muffler; *P*, blower; *A*, acid trap; *B* and *C*, Williams water-absorbers; *V*₁ and *V*₂, 2-way valves; *D*₁ and *D*₂, carbon dioxid absorbers; *E*₁ and *E*₂, air-dryers; *F*, sodium bicarbonate can; *J*, by-pass; *R*, valve; *K*, air moistener; *L*, oxygen cylinder; *I*, ingoing air-pipe; *S*, spirometer; *T*₁ and *T*₂, thermometers; *M*, manometer; *U*, spiral spring; *H*, pneumograph.

infant, contains a normal amount of nitrogen, and is deficient in oxygen. By means of a rotary pump, the air is carried from the chamber and forced through sulphuric acid which absorbs the water, then through soda lime to remove the carbon dioxid; oxygen is next introduced and when the air returns to the chamber it is free from carbon dioxid and water and contains a normal percentage of nitrogen and oxygen. A scheme of this respiration apparatus, giving in considerable detail some of the special connections, may be seen in Figure 1.

48. Benedict, F. G., and Talbot, F. B.: Carnegie Institution of Washington, Publication No. 201, 1914.

METHOD OF RECORDING THE DEGREE OF MUSCULAR REPOSE

Special care was taken to secure graphic records of the degree of muscular repose of the infant, and each experiment in the entire series of some 1,200 periods, with about eighty infants, was accompanied by a graphic registration of the degree of muscular repose. This was accomplished by resting one end of the crib on a knife-edge bearing and suspending the other on a spiral spring, so that even the slight changes in the center of gravity of the infant would alter the tension on the spring. One end of a pneumograph was attached to the crib and the other end to the wall of the chamber, the pneumograph thus being parallel to the spiral spring. The slightest lengthening or shortening of the pneumograph produced a change in the tension of the confined air, these varying air tensions being transmitted by a tube through the walls of the chamber to a delicate tambour and pointer which gave graphic records on a kymograph drum. It is only necessary here to give one characteristic tracing, illustrating the records obtained by this method as to the degree of muscular repose. This curve, which is shown in Figure 2, was obtained Jan. 28, 1914, with G. M., an infant weighing 3.73 kg.

At the bottom of the figure is shown the record of the sensitivity test which precedes each experiment. In these tests, weights equal to the weight of the infant are placed in the crib; a 50-gm. weight is then dropped from a height of 21 cm. so as to strike the crib a blow at approximately 32 cm. from the knife-edge bearing on which the crib rests, thus giving an impulse to the crib, the vibrations gradually slowing down. Tests are made with the kymograph set first at slow speed and then at fast speed. In the record of the experimental period, the major movements are shown by the larger amplitude. It will be seen that the infant quieted down sufficiently to begin the first period of the experiment at 3:05 p. m. Aside from the slight movements at the end of the period, the infant was very quiet until 3:28 p. m. In the period from 3:28 p. m. to 3:59 p. m., there were several major movements and toward the end of the next period the infant was obviously very restless. This curve is of particular interest in that it shows in the period from 4:23 p. m. to 4:50 p. m. the movements of the crib incidental to hiccoughs. Indeed, it is possible so to adjust the sensitivity of the crib as to record the respirations.⁴⁹

At first the infant was observed through the window in the cover of the apparatus to see whether or not he was quiet. While the ocular method of recording changes in position and the activity of an infant

49. Benedict, F. G., and Talbot, F. B.: Carnegie Institution of Washington, Publication 201, 1914, p. 58 (Fig. 6).

is much to be preferred to the terse statements usually accompanying reports of metabolism experiments to the effect that the animal, infant or person was "quiet," "fairly quiet" or "restless," yet such observa-

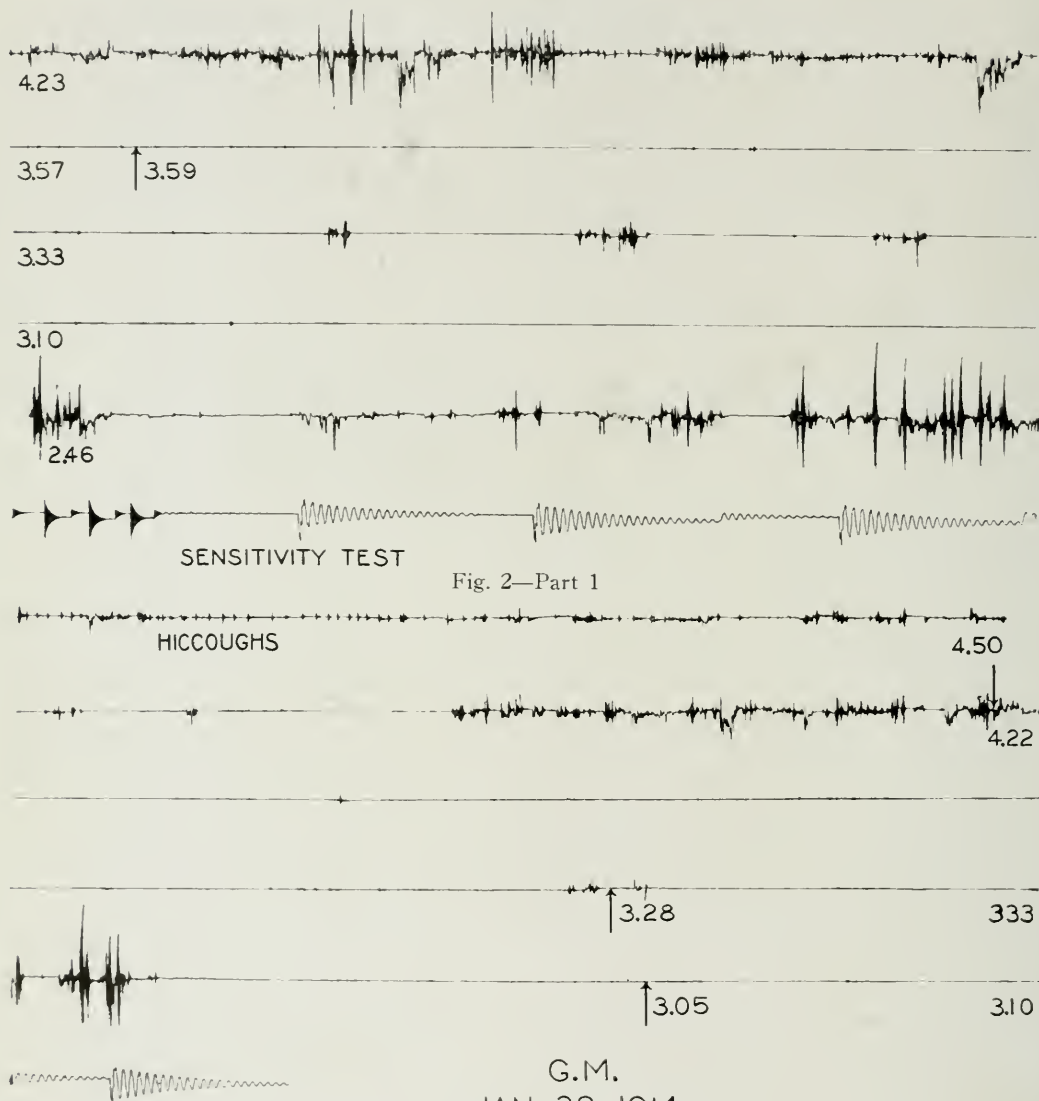


Fig. 2—Part 2

Fig. 2.—Typical kymograph curve, showing sensitivity test and records of muscular activity.

tions cannot be relied on. We have repeatedly seen experimental periods when a careful observer, even though watching the infant continuously, was unable to record a perceptible movement other than

those of respiration, and yet the suspended crib, pneumograph and tambour have recorded distinct and persistent muscular tremors, accompanied in all cases by an increasing pulse-rate and increased metabolism as measured by the carbon dioxid production and oxygen



Fig. 3.—General view of the infant respiration apparatus. In the foreground is the respiration chamber showing the crib inside. The cover of the chamber rests on the floor, and through the glass window may be seen the carpieces of the stethoscope used for recording the pulse-rate. On the shelf in front of the chamber are the tambour and kymograph for the graphic records of movements. Directly behind the chamber are the hygrometer, the gas meter immersed in water, and the cylinder of oxygen, while in the rear the spirometer may be seen at the right and the sulphuric acid and soda lime containers of the absorbing system at the left. In the corner of the room is the balance for weighing the absorbing system.

consumption. The visual estimation was therefore discontinued as being too inaccurate and unreliable a record of the degree of quiet.

The length of a period of observation depends altogether on the muscular repose of the infant, as only quiet periods, accompanied by

a low pulse-rate, are of value. With a small, quiet infant, the periods may vary in length from twenty to thirty minutes, but with a large infant they may be as short as fifteen minutes.

The respiration apparatus as installed in the Children's Department of the Massachusetts General Hospital is shown in Figure 3. It consists of the respiration chamber, with oxygen supply, meter, balances for weighing, air-purifying apparatus, barometer and tambour and kymograph for recording the degree of muscular repose.

WARD CRIB RECORDER

The relationship observed between the graphic tracings of the muscular activity and the catabolism indicated the possible value of recording the activity of the infant throughout the day when it was not inside the respiration chamber. Accordingly, to assist in settling

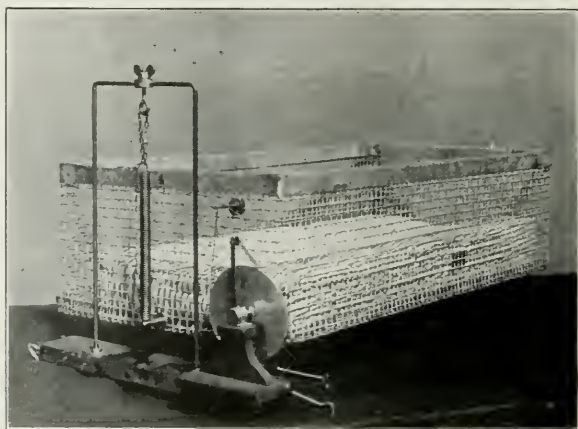


Fig. 4.—Ward crib recorder.

some complicated problems of nutrition, a special apparatus, embodying the suspended crib principle, was devised and set up in the children's ward of the hospital in order to obtain a continuous graphic record of the muscular activity of the infant (Fig. 4).

In this apparatus the wire crib rests at the rear end on two steel points fitting into steel cups. The front end is suspended by a spring with link chain adjustment for height. At the right of the front end is an aluminum wheel attached to a revolution counter. A fine thread fits in a groove on the edge of this wheel. One end of this thread is attached to the upper end of the cage and the other end to a fine spiral spring, projecting to the right of the revolution counter. Each movement of the cage in a vertical direction moves the revolution counter, and as the cage descends, the fine spring keeps the tension on the

thread tight. The pawl on the top prevents backward motion of the wheel and the pawl-standard serves as a pointer to read fractions of the circumference of the wheel.

METHOD OF RECORDING THE PULSE-RATE

Previous experiments with adults in the Nutrition Laboratory, in which the large respiration chambers were used, showed a striking relationship between the pulse-rate and the metabolism. Attempts were accordingly made to secure accurate pulse-records in our observations with infants. For this purpose we attached the bell of a small Bowles stethoscope to the infant over the apex-beat of the heart by means of strips of adhesive plaster. A rubber tube connecting with the bell led to a pipe in the wall of the chamber, a piece of rubber tubing and earpieces being attached to the outer end of the tube. Even with a total length of some 2 or 3 meters from the bell to the earpieces, it was possible to count the pulse-rate of the weakest infant. Throughout the entire period of observation, the pulse-rate was recorded every two minutes by an assistant who made this her sole duty.

We are far from satisfied with this as a permanent method for securing a record of the pulse-rate, and it is our hope, in connection with the hospital or with the laboratory, to secure records either with the string galvanometer or with the Bock-Thoma oscillograph. It is clear that the records of the pulse-rate should be more objective than they can be even with a specially detailed assistant.

SELECTION OF SUBJECTS

The infants studied were either from the Children's Department of the Massachusetts General Hospital or from the Boston Lying-In Hospital. The routine histories, records of the physical examinations, notes regarding the urine, stools, blood and temperature, the pulse and respiration charts, and detailed records of the food were kept for all of the infants. The Wassermann reaction and the von Pirquet skin tests were also made in many cases. It does not seem desirable to publish the detailed hospital record of each infant that came under observation, especially since most of the evidence is negative as to whether or not an infant is normal. The clinical status of each infant is, however, given in Table 13.

In this table the term "infantile atrophy" is applied to the condition of an emaciated infant with such severe indigestion that it is unable to digest weak mixtures of cow's milk, with no gain in weight, and with a subnormal body-temperature. The convalescent stage of infantile atrophy is that in which the same infant subsequently begins to digest its food and to gain weight and has a normal temperature. Under-

TABLE 13.—CLINICAL STATUS OF INFANTS STUDIED

Name	Age During Metabolism Observation	Clinical Status
F. B.	5½ mos...	Convalescent stage infantile atrophy.
M. A.	9 mos...	Under weight, splenic tumor, with anemia.
J. B.	5 mos...	Congenital syphilis, convalescent stage infantile atrophy.
L. B.	4 mos...	Under weight.
L. R. B.	4-4½ mos...	Normal infant.
A. C.	1½ mos...	Slightly under weight.
M. C.	4 mos...	Normal infant or slightly under weight.
A. D.	4-5 mos...	Convalescent stage, infantile atrophy.
M. D.	2-3 wks...	Normal infant.
R. E.	4½ mos...	Under weight or slightly under expected weight.
E. F.	3 mos...	Normal infant.
E. G.	10 mos...	Normal infant.
E. K.	17 mos...	Much under weight; rachitis, recovering from broncho-pneumonia.
F. K.	7 mos...	Under weight.
A. L.	3½-4 mos...	Under weight.
E. L.	4 mos...	Under weight, otitis media.
R. L.	6½-9 mos...	Approximately normal; later, under weight.
D. M.	11 mos...	Much under weight, rachitis.
F. M.	4-5 mos...	Under weight, congenital syphilis.
J. M.	8 mos...	Under weight, otitis media, rachitis.
M. M.	4½ mos...	Under weight following an acute indigestion.
E. N.	6-6½ mos...	Under weight.
L. O.	5-6 mos...	Infantile atrophy.
J. P.	6½-7 mos...	Under weight, gaining weight rapidly.
W. P.	5-5½ mos...	Under weight.
D. Q.	4½ mos...	Under weight.
E. R.	3 mos...	Under weight (slightly).
K. R.	4 mos...	Infantile atrophy.
A. S.	3 mos...	Normal infant, weighing more than the average.
E. S.	5 mos...	Infantile atrophy.
E. H. S.	2½-4 mos...	Infantile atrophy.
G. S.	2½ mos...	Under weight.
J. S.	5-6 mos...	Infantile atrophy (?) (temperature not subnormal).
P. S.	12 mos...	Under weight.
H. T.	5½ mos...	Normal infant, weighing more than average.
J. V.	3½-9 mos...	Prematurity; congenital syphilis; infantile atrophy in subnormal temperature and convalescent stage.
P. W.	7 mos...	Normal infant.
New Series		
R. A.	7 mos...	Moderately underweight.
E. C.	2½ mos...	Moderately under weight with indigestion.
H. C.	5 mos...	Much under weight.
O. C.*	5 hrs.-3 das.	Normal infant.
R. C.*	1-2 days...	Normal infant.
T. C.	8½-9 mos...	Much under weight.
B. D.	2 mos...	Normal infant. Breast fed.
F. D.	2½ mos...	Congenital syphilis. Normal weight.
N. D.	7 mos...	Moderately under weight.
R. D.*	2-5 days...	Normal infant of average weight.
B. F.	7 mos...	Moderately under weight.
U. H.*	3-28 hours.	Normal infant.
T. K.*	7-32 hours.	Normal infant.
L. L.	2-2½ mos...	Normal infant.
E. M.	8 mos...	Moderately under weight.
G. M.	6-6½ mos...	Much under weight. Eczema. Indigestion.
C. N.	4½ mos...	Eczema. Much under weight with indigestion.
I. N.	2-4 days...	Normal infant.
J. O.	4½ mos...	Pyloric spasm. Indigestion. Much under weight.
E. P.	11-14 days...	Normal infant.
F. R.	1-11 days...	Normal infant. Much above average weight.
I. R.	6-7 days...	Normal infant.
R. S.	9½ mos...	Normal infant. Much over average weight.

* These infants were obtained through the courtesy of the visiting physician of the Boston Lying-In Hospital, Dr. Charles Montraville Green.

weight infants are those who are 0.5 kg. or more below the average weight for their respective ages, but whose digestion is not so severely deranged as those with infantile atrophy. This group includes all infants not classified as normal, or with infantile atrophy, or in the convalescent stage of infantile atrophy.

DISCUSSION OF RESULTS

In all of the researches carried out in the Nutrition Laboratory, particularly in studying pathologic cases, the want of suitable and adequate control data for comparison has been evident. With infants, particularly, the absence of normal controls is unfortunate. This led us to believe that our best service to pediatrics would be to determine the normal metabolism of infants. Accordingly, while a few observations were made on distinctly pathologic cases other than atrophic, our data were secured for the most part with normal or underweight infants.

One of the most important problems in such an investigation is the relationship between muscular repose and metabolism. In our first communication to this journal, we emphasized the importance of this relationship and pointed out the great service rendered by the graphic registration device for recording the muscular movements of the infant. Our consistent use of this device in all of our experiments furnished us with data in regard to the relationship between muscular repose and metabolism, which was accordingly made the subject of special study in this investigation.

In this research, also, it was hoped that some information would be gained as to the cause for variations in the metabolism of the infant; with this in view, a study was made of the possible relationships between the metabolism and the body-surface and the metabolism and the active mass of protoplasmic tissue.

1. Pulse-Rate

The careful observations of pulse-rate made while the subjects were inside the respiration chamber verified completely the twelve-hour observations made in the ward and published in our earlier paper. These showed very considerable fluctuations in the pulse-rate coincident with changes in muscular activity, such as change in body position, particularly in crying and immediately after nursing, so far as the movements inside the respiration chamber approximated those noted in the ward. For an elaborate series of observations on the pulse-rate as affected by the muscular activity incidental to a night's sojourn in the wards, our earlier paper may be consulted, as well as a number of records given more recently in the Carnegie Institution of Washington publication.

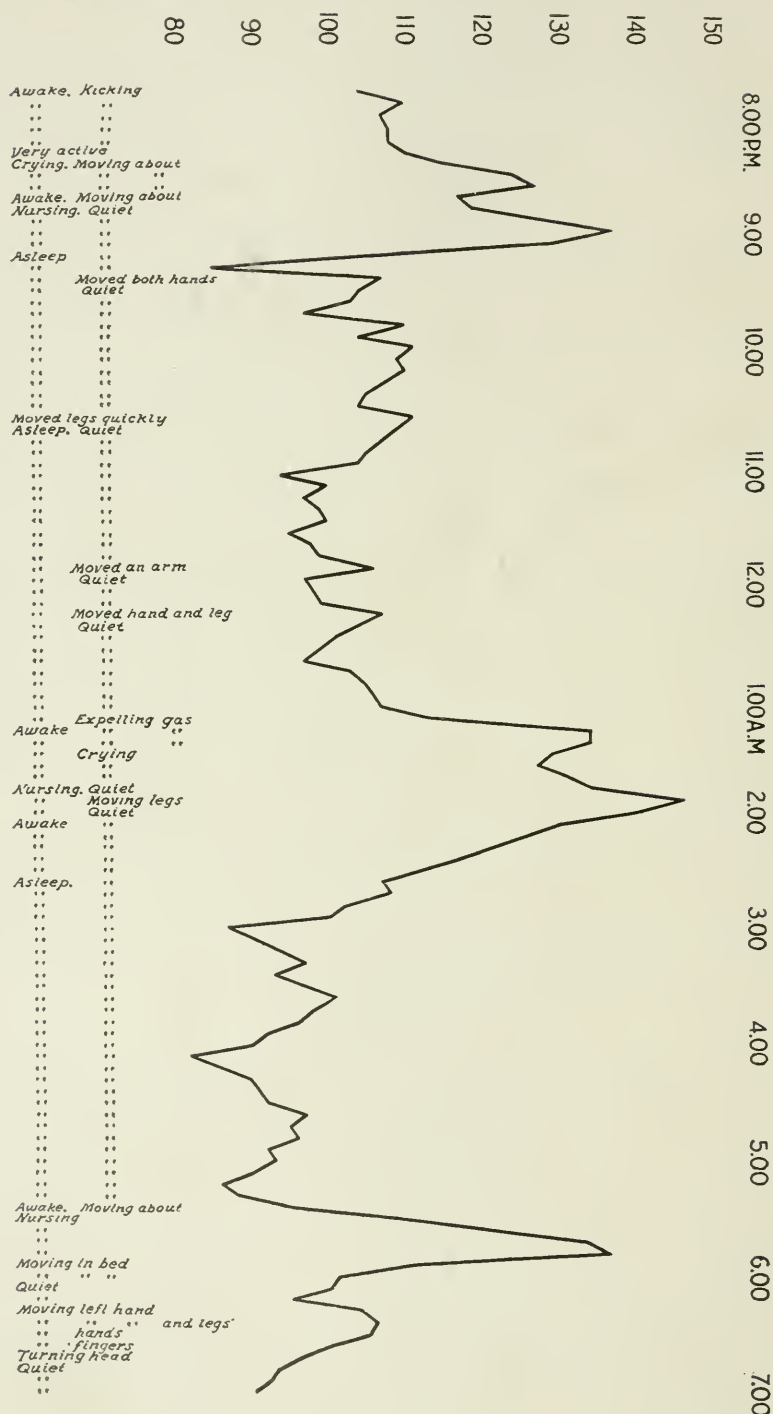


Fig. 5.—Pulse-rate curve for Tremballe, July 12, 1911. Age, 5 months; weight, 5.7 kg.

The surprising changes in pulse-rate found in the course of an ordinary night's sleep in the ward are shown in Figure 5 by the typical curve for the 5-months-old infant, Tremballe. Accompanying the curve are statements with regard to the condition and activity of the child. Tremballe was under observation in the ward from 7:40 p. m. until about 7 a. m., and for the greater part of this time was asleep. The pulse-rate varied from a maximum of 147 to a minimum of 83. During the latter part of the night the minimum record showed an average of not far from 90. An immediate and rapid effect on the pulse following changes in muscular activity is strikingly shown with this infant in every instance.

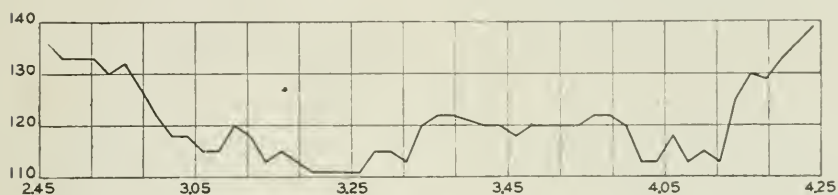


Fig. 6a

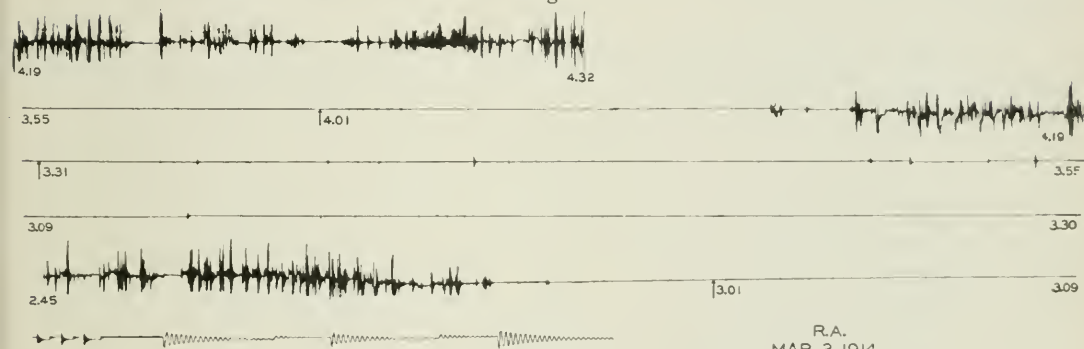


Fig. 6b

R.A.
MAR. 2, 1914.

Fig. 6.—Pulse-rate and kymograph curves for R. A., March 2, 1914.

2. Relationship Between Pulse-Rate and Muscular Activity

While the observations made in the ward during the night experiments in 1911 showed conclusively the intimate relationship between pulse-rate and activity, this is even more strikingly brought out by the kymograph pictures obtained while the infant was inside the respiration chamber. With each change in bodily activity, there was obviously a noticeable change in the course of the kymograph record, and by means of frequent pulse-counts, we were able to make sharp comparisons between these two factors. A curve showing graphically the pulse-counts obtained in a typical experiment with R. A. on March 2, 1914, is given in Figure 6. For comparison, the kymograph record, somewhat reduced, is also given.

In comparing the two curves, we find that the period of considerable activity from 2:45 p. m. until about 2:58 p. m. is accompanied by a high pulse which fell rapidly as the infant quieted down. From 3:01 p. m. to 3:30 p. m., the kymograph curve shows a straight line, with but one or two slight movements. From 3:31 p. m. to 3:55 p. m., there is distinct evidence of slight restlessness, which is also apparent in the increased pulse-rate, this period being followed by complete repose from 3:55 p. m. to about 4:10 p. m., and a lowering of the pulse-rate. From that time until the end of the experiment, there is great activity and disturbance, with a rapidly rising pulse-rate. It is thus seen that the kymograph curve and the pulse-rate curve follow each other with great regularity.

3. Relationship of the Muscular Activity, Pulse-Rate and Metabolism

The noticeable influence of even minor muscular activity on metabolism makes it important to note that in all experiments in which the basal metabolism is to be determined, that is, in experiments that

TABLE 14.—COMPARISON OF THE PULSE-RATE, METABOLISM, AND MUSCULAR ACTIVITY IN OBSERVATION WITH M. M., JUNE 5, 1913

Period	Total Heat- Production per 24 Hours	Pulse- Rate	Activity
3:12 p. m. to 3:40 p. m.*	365	107	V
3:40 p. m. to 4:10 p. m.	276	93	I
4:10 p. m. to 4:31 p. m.	307	96	III
4:31 p. m. to 4:58 p. m.	288	90	II
4:58 p. m. to 5:23 p. m.	367	113	VI

* Preliminary period.

may subsequently be employed for comparison of normal individuals with pathologic cases, only periods of complete muscular repose should be used. It is obviously impossible to compare a quiet, resting, normal child with a sick, restless child, or vice versa. The difficulties incidental to securing such periods are known only to those who are actively engaged in this sort of experimenting, for a very large percentage of the results of experimental work may not be used, owing to changes in the extraneous muscular activity. Writers have, as a rule, attempted to indicate in a general way the results of certain experiments which cannot properly be included in comparisons by recording in some general terms the degree of activity of the child, stating whether it is awake or asleep, or comparatively quiet, or quiet,

etc. In recent years Schlossmann and Murschhauser have adopted a more elaborate system of ocular records, stating exactly what the infant is doing. After comparing the various methods of recording the degree of muscular repose, we have definitely adopted the suspended crib and kymograph.

It is clearly impracticable to reproduce in this publication all of the kymograph curves secured in our researches, but a comparison may be made of the muscular activity, the pulse-rate, and the metabolism in a typical experiment—that with M. M. on June 5, 1913—by reference to Table 14. In this table are given a record of the pulse-rate, the metabolism computed on the basis of the total heat output for twenty-four hours, and an estimate of the activity based on the following classification:

- I. Very quiet, probably asleep.
- II. Slight movements, few in number.
- III. Some activity, but generally quiet.
- IV. Moderately active.
- V. Distinctly active.
- VI. Very active, most or all of the time.

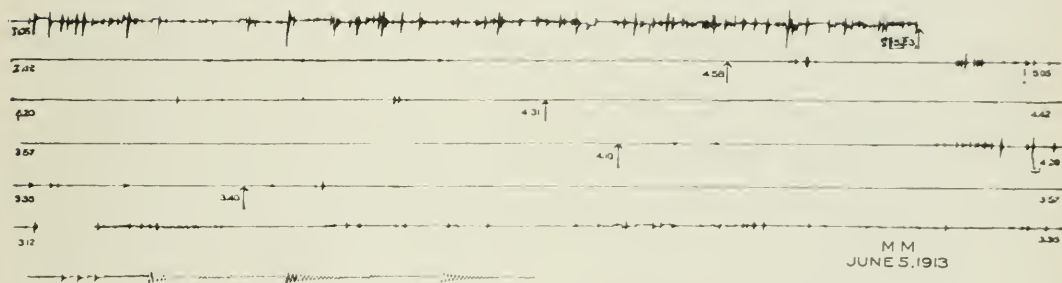


Fig. 7.—Kymograph curve for M. M., June 5, 1913.

The kymograph curve for the same experiment, which is reproduced in Figure 7, will give an illustration of the method of estimation we are using. This curve has certain striking points, inasmuch as the minimum and maximum activity are very well shown. During the preliminary period from 3:12 p. m. to 3:40 p. m., the infant was somewhat restless, quieting down sufficiently about 3:35 p. m. to justify the beginning of a new period at 3:40 p. m. As a matter of fact, the infant was so quiet in the next period that the activity can be characterized as I (Table 14). The activity in the last period, that is, that from 4:58 p. m. to 5:23 p. m., was sufficiently great to be classified as VI. This curve shows clearly the futility of attempting to graduate by kymograph records the exact degree of the activity and the heat-production, for although the curve appears to indicate

that the activity in the last period (from 4:58 p. m. to 5:23 p. m.) was much greater than that in the preliminary period from 3:12 p. m. to 3:40 p. m., the metabolism is very nearly the same and the pulse-rate is only 6 beats higher in the last period. This also justifies the statement that the measurements obtained in preliminary periods are not sufficiently reliable to admit of extended discussion. The fact that no greater metabolism is shown in the last period than in the preliminary period, although the activity appears to be greater, should therefore be considered as a deduction based on single measurements in two individual periods, either of which may be liable to error. Furthermore, when comparing the pulse-rates it should be stated that although the average pulse-rate in the preliminary period was 107, the individual counts ranged from 95 to 120, while the pulse-rates in the last period, although the average was 113, actually varied from 93 to 124. Discrepancies such as these serve again to emphasize the fact that only periods of complete muscular repose can logically be used in discussing infant metabolism.

4. Significance of the Relationship

From the preceding discussion the conclusion may be drawn that only periods of complete muscular repose may be used in comparing the results obtained with different individuals and with the same individuals on different days. The total catabolism of the infant is the resultant of two factors: first, the metabolism due to the internal activity incidental to circulation and respiration and the general muscle tonus of the body, that is, maintenance metabolism; second, the metabolism due to the external muscular activity, which may vary from slight movements of the hand or fingers to violent movements incidental to severe crying.

The external muscular movements are recorded with considerable fidelity on the kymograph drum by means of the registering apparatus described, but we have seen that this record does not give a comparative picture of the degree of activity of different infants. Consequently for comparing the maintenance metabolism only periods in which the external muscular activity is eliminated should be used, since in the last analysis, knowledge with regard to internal muscular activity is desired, uncomplicated by the increased metabolism due to external muscular activity. We believe that our evidence justifies us in asserting that we have two admirable indices for securing these ideal conditions of muscular repose for comparison, first, the graphic records obtained with the kymograph, and second, the pulse-rate. For comparing the metabolism of different infants, therefore, only those periods with records of complete muscular repose and with a minimum pulse-rate can legitimately be employed.

5. Relationship between Pulse-Rate and Metabolism

From the general pictures of the kymograph curves and the pulse-curves, one may infer that the pulse-rate follows closely the muscular activity. Furthermore, since it has been shown that the relationship between the metabolism and the kymograph curves is comparatively constant, it is reasonable to expect that the pulse-rate will follow the metabolism. That this latter relationship is usually more nearly constant than the relationship between the metabolism and the record of the muscular activity is clearly indicated in a number of observations in which the kymograph record showed a complete absence of extraneous muscular activity while the pulse-records showed fluctuations.

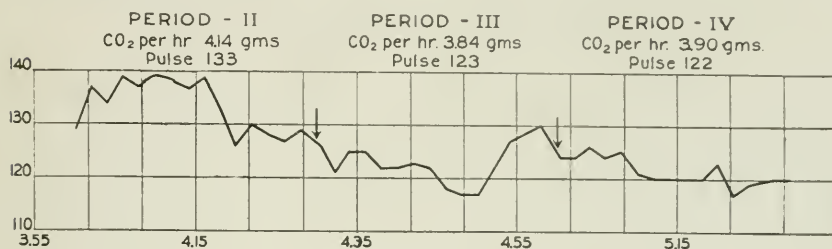


Fig. 8a

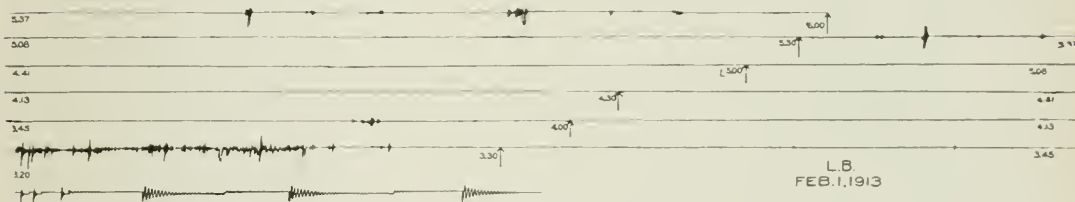


Fig. 8b

Fig. 8.—Pulse-rate and kymograph curves for L. B., Feb. 1, 1913.

An excellent illustration of this may be seen in the pulse and kymograph curves which were obtained in the observation of Feb. 1, 1913, with the infant L. B. (Fig. 8). Thus between 4 p. m. and 5:30 p. m., one may assume that the activity was essentially of Grade I, that is, minimum. Nevertheless the pulse-rate is considerably higher in the period between 4 p. m. and 4:30 p. m. than in the two following periods, as is shown by the pulse-curve and the figures for the pulse-rate per minute. As a matter of fact, the total metabolism is likewise higher in the first period as is evidenced by the carbon dioxide output per hour which is given on the pulse-curve. In this curve, therefore, which excludes the extraneous activity, we find the pulse-rate following very closely the total metabolism. While the kymograph

curve did not indicate muscular activity, nevertheless the pulse-rate gave evidence of an increased internal activity.

6. Basal Metabolism of Infants Studied

In the beginning of this research on infant metabolism, one of the fundamental questions which presented itself to us with special force was as to what may be considered the normal basal metabolism of infants. Consequently we made it our aim to study as many infants as possible and to secure a sufficient number of periods of complete repose on a sufficient number of days to establish beyond reasonable doubt the basal metabolism of each infant. The infants secured for these observations varied sufficiently in age, weight, height, and sex to permit a comparative study of the results as to the constancy or lack of constancy in the metabolism.

A. Selection of Data Used for Comparison

From the data obtained a table has been compiled which gives the average results of the periods with each infant in which the metabolism was at a minimum (Table 15). The selection of the periods was based on the records of the pulse-rate and the muscular activity, only such periods being used as showed a normally low pulse-rate and practically no muscular activity, that is, those characterized as I or II. Of the eighty-three infants studied thus far in this research, but sixty were used in the comparison of the metabolism of different infants and but 360 periods out of the 1,250 periods were available for the comparison. The data are arranged according to the increasing weights of the infants. Since with one infant, J. V., the studies continued over a period of several months, the average minimum metabolism is given for periods secured at an early age, and again for periods obtained several months later. Various bases of comparison may be used, but in this table the infants have been compared on the basis of the energy transformation in twenty-four hours.

In employing the data in Table 15 for the discussion of the fundamental questions considered, it is necessary to emphasize the fact that the amount of material and the method of its selection justify its use for a basis of comparison.

The number of infants (sixty in all) permits extended comparison and discussion.

Furthermore, the data are sufficiently extensive for each subject, as an examination of the table will show that in all but two instances, at least two periods are used for securing the average value for each infant; in other words, the values were determined in duplicate. In many cases the number of periods for comparison greatly exceeded

this; for example, in one instance twenty-two periods were available for averaging.

Obviously no infant lives on a minimum metabolic plane throughout the entire twenty-four hours; indeed, but a small proportion of the total number of the experimental periods could be utilized for this important comparative study. Nevertheless, since in but two instances was it necessary for us to rely on the computation of the minimum metabolism of the infant from one experimental period, and in only one other instance were our data limited to those secured in two periods on one day, we believe that we have obtained a reasonably accurate estimate of the minimum metabolism of each infant which justifies critical study and comparison.

B. Minimum Influence of Food

In discussing our results, the criticism can be raised that one of the factors outlined in our definition of basal minimum metabolism was not so strictly observed in this study as could be desired in that the infants were rarely in the postabsorptive state, since the observations were for the most part made from one to one and a half hours after the ingestion of food.

It has clearly been shown in experiments on men and animals that the ingestion of a mixed diet results in an increased metabolism. When isolated nutrients are ingested, the greatest increase has been observed with protein. With fat there is relatively but little, if any, increase. With carbohydrates, while investigators differ as to the quantitative relationships, it has been observed with men in this laboratory that cane-sugar and levulose may stimulate the metabolism to a degree comparable with that resulting from the ingestion of an equivalent weight of protein. On the other hand, lactose—the chief carbohydrate in the diet of infants—has a minimum influence on the metabolism.

This criticism of our experiments has, therefore, considerable theoretical importance, but practically we must consider the fact that the diet of the infant is of such a character as to produce a minimum amount of increase in the metabolism. With infants a large proportion of the protein ingested—some 60 per cent. or more—may be stored in the body, and Rubner has shown that this storage does not affect the total metabolism. Since the protein ingested by the infant rarely exceeds 15 per cent. of the total energy requirement of the body,⁵⁰ it can be seen that we may expect from this nutrient only the minimum influence on the heat-production of infants. Fat has admittedly but a slight influence, while the predominating carbohydrate—milk-sugar or lactose—has likewise only a minimum influence.

50. Rubner: Sitzber. k. Preuss. Akad. Wissensch, 1911, xx, 440.

TABLE 15.—MINIMUM—

Subject	Sex*	Body-Weight Without Cloth- ing kg.	Height cm.	Age	Days Included in Average	Peri- ods Aver- aged	Carbon Dioxid per Sq. Meter (Meeh) per Hr.† gm.
J. V.	♀	1.94	47	3½ months	2	3	12.1
E. H. S.	♀	2.96	51	3½ months	5	8	11.6
A. C.	♀	2.99	..	1½ months	3	8	9.7
E. S.	♀	2.99	..	5 months	3	6	14.0
A. D.	♀	3.16	56	4½ months	5	15	13.0
K. R.	♂	3.17	56	4 months	2	4	12.1
A. L.	♀	3.18	53	4 months	2	2	12.4
L. O.	♂	3.18	..	6 months	7	12	15.3
J. B.	♂	3.23	..	5 months	2	4	13.3
G. S.	♂	3.30	..	2½ months	3	5	12.1
R. D.	♀	3.31	47	3 days	4	5	7.1
J. V.	♀	3.38	53	8½ months	3	3	16.7
H. C.	♀	3.42	55	5 months	2	4	15.2
O. C.	♂	3.45	51	2 days	3	6	7.8
J. O.	♀	3.53	57	4½ months	2	6	13.8
T. K.	♂	3.60	53	19 hours	2	3	7.5
I. N.	♂	3.65	52	3 days	3	5	7.5
F. M.	♂	3.65	..	4½ months	3	5	15.4
E. C.	♂	3.70	57	2½ months	3	5	13.9
E. P.	♀	3.71	51	12½ days	2	4	7.9
G. M.	♂	3.73	58	6 months	4	8	15.2
I. R.	♂	3.89	52	6½ days	2	2	10.3
M. D.	♂	3.99	..	17 days	2	4	9.2
U. H.	♂	4.00	53	15 hours	2	2	7.4
L. B.	♀	4.04	..	4 months	3	8	13.2
R. C.	♀	4.13	51	37½ hours	2	4	7.9
E. L.	♂	4.15	59	4 months	1	2	14.0
W. P.	♂	4.31	..	5 months	2	6	14.6
F. R.	♂	4.40	52	6 days	6	8	8.6
J. S.	♂	4.41	63	5½ months	5	7	15.6
E. R.	♂	4.49	55	3 months	3	5	12.0
T. C.	♂	4.72	66	8½ months	5	10	15.5
C. N.	♀	4.74	63	4½ months	2	6	13.6
F. D.	♂	4.80	59	2½ months	1	2	12.4
F. B.	♂	4.87	60	5½ months	4	13	15.7
B. D.	♀	4.90	58	2 months	2	4	10.5
R. E.	♂	5.04	60	4½ months	3	7	12.2
L. L.	♂	5.13	57	2½ months	10	13	10.6
D. M.	♂	5.18	66	11 months	2	2	15.0
D. Q.	♂	5.28	62	4½ months	2	4	11.9
E. N.	♀	5.40	66	6 months	7	22	13.9
J. P.	♂	5.45	63	7 months	4	7	15.3
M. M.	♀	5.47	62	4½ months	3	7	10.6
J. M.	♂	5.63	62	8 months	2	6	18.2
M. A.	♂	5.67	68	9 months	4	9	12.9
F. K.	♂	5.71	65	7 months	6	8	14.2
B. F.	♀	5.72	64	7 months	2	5	14.9
L. R. B.	♀	5.99	64	4 months	4	11	11.3
A. S.	♂	6.02	63 (?)	3 months	1	1	10.6
M. C.	♀	6.17	63	4 months	3	7	11.9
E. M.	♂	6.19	63	8 months	2	2	18.7
R. A.	♀	6.42	65	7 months	2	3	12.4
N. D.	♀	6.79	67	7 months	3	5	12.3
P. S.	♂	6.80	67	12 months	3	10	14.4
E. F.	♂	7.07	62	3 months	2	2§	10.2
P. W.	♂	7.11	64 (?)	7 months	2	5	14.2
R. L.	♂	7.58	71	8½ months	5	8	13.9
E. K.	♂	8.03	73	17 months	1	2	14.2
H. T.	♂	9.33	75 (?)	5½ months	1	1	12.4
E. G.	♂	9.37	74	10 months	3	5	11.4
R. S.	♂	9.94	74	9½ months	2	4	13.4

* In this column ♀ means female and ♂ male.

† In accordance with the usage of European writers, we give these values, although we

‡ See page 15.

§ The activity estimated for these two periods was II and III, respectively.

Oxygen per Sq. Meter (Meeh) per Hour gm.	Heat Produced					Average Rectal Temperature During Respiration Periods		Pulse- Rate
	Per 24 Hrs. cals.	Per Kilo- gram per 24 Hours cals.	Per Square Meter per Twenty-Four Hours					
			How- land† cals.	Lissauer $\frac{3}{10.3 \sqrt{w}}$ cals.	Meeh $\frac{3}{11.9 \sqrt{w}}$ cals.	°C	°F	
10.8	164	85	984	1,032	882	129
9.6	194	65	891	906	783	36.8	98.2	109
8.0	163	55	756	759	660	37.2	98.9	126
11.0	225	75	1,036	1,048	911	36.5	97.7	107
10.7	229	72	1,010	1,026	895	36.5	97.7	114
10.2	213	67	936	960	829	36.6	97.8	103
10.7	226	71	996	1,020	876	36.8	98.3	107
12.1	260	82	1,154	1,172	1,008	36.9	98.5	106
10.2	223	69	978	996	854	36.1	97.0	95
10.0	216	65	931	946	818	36.9	98.4	119
6.8	146	44	632	641	554	37.1	98.8	110
13.4	297	88	1,264	1,280	1,108	37.3	99.1	126
12.6	280	82	1,184	1,199	1,039	37.3	99.2	113
8.0	168	49	703	714	618	36.9	98.4	129
11.2	255	72	1,051	1,069	925	36.8	98.2	104
7.0	158	45	655	664	575	37.0	98.6	105
8.0	174	48	702	715	616	36.9	98.4	104
13.0	300	83	1,219	1,238	1,064	37.1	98.8	118
11.3	267	72	1,068	1,085	939	37.4	99.4	122
7.5	169	46	672	683	590	36.8	98.3	119
12.7	299	80	1,186	1,205	1,041	36.8	98.2	112
8.6	211	54	810	827	715	36.8	98.3	127
8.2	196	49	738	756	656	37.0	98.6	127
6.8	167	42	630	643	556	37.1	98.7	114
10.6	272	67	1,020	1,041	901	36.9	98.5	124
7.6	186	45	684	701	606	37.1	98.8	108
12.3	306	74	1,128	1,152	995	37.2	99.0	127
11.6	303	70	1,076	1,104	962	36.8	98.2	96
8.0	207	47	732	752	649	37.2	99.0	121
11.9	319	72	1,114	1,152	997	36.9	98.5	111
11.0	283	63	979	1,013	873	37.2	98.9	116
12.9	354	76	1,194	1,230	1,062	37.0	98.6	109
12.0	330	70	1,097	1,136	982	36.9	98.4	116
11.0	303	63	999	1,033	892	37.7	99.8	115
13.1	370	77	1,211	1,257	1,082	37.2	98.9	111
9.8	274	57	898	927	802	37.7	99.8	122
11.3	324	64	1,035	1,070	919	37.1	98.7	114
9.4	269	52	844	878	759	37.3	99.1	119
12.5	369	71	1,152	1,188	1,034	37.3	99.1	119
10.1	305	57	930	972	846	37.3	99.1	101
11.7	353	66	1,069	1,117	962	37.1	98.7	111
13.0	387	70	1,152	1,207	1,039	36.8	98.3	105
9.7	285	52	854	891	770	36.8	98.2	96
15.1	467	83	1,368	1,432	1,239	37.2	98.9	112
11.7	356	63	1,037	1,085	939	36.9	98.5	105
12.6	381	67	1,107	1,158	1,003	37.2	98.9	109
12.3	386	68	1,115	1,165	1,016	37.1	98.7	109
10.4	331	55	923	973	844	37.2	99.0	106
9.5	305	51	840	888	774	37.3	99.1	113
10.1	333	54	912	967	837	37.1	98.8	103
16.2	535	87	1,452	1,540	1,334	37.4	99.4	130
10.5	358	56	940	1,002	868	37.4	99.3	118
11.1	381	56	965	1,032	893	37.2	99.0	100
13.3	453	66	1,133	1,219	1,058	36.8	98.2	100
8.7	311	44	756	828	708	37.1	98.8	111
12.2	439	62	1,061	1,147	998	37.1	98.8	120
12.2	455	59	1,038	1,140	991	37.4	99.4	115
12.9	497	62	1,092	1,212	1,044	37.7	99.9	105
9.5	420	45	816	912	797	37.2	98.9	101
11.4	479	51	922	1,046	907	37.2	98.9	106
11.5	531	53	971	1,115	965	37.3	99.1	108

believe they are peculiarly liable to misunderstanding and hence their use is unfortunate.

On these grounds, therefore, one would conclude that the total nourishment of the infant consists of material which for the most part does not tend to stimulate the metabolism greatly. On the other hand, so keen an observer as Schlossmann⁵¹ states that the effect of the ingestion of food probably persists for some eighteen hours. Practically all of the investigators in metabolism have concluded that with adults, unless the diet is abnormally rich in protein, the metabolism reaches the basal line twelve hours after the last meal.

In our studies, while it was impracticable to secure the metabolism on all of the infants eighteen hours after the last meal, an effort was made to find out the length of time required to obtain the minimum basal metabolism after feeding milk. To this end some five or six infants were studied 1, 2½, 5, 9, 12, 18 and 21 hours after food. The difficulties in securing ideal periods of rest exactly coincident with definite periods of time after the ingestion of food are sufficiently obvious to need no special comment here; it is only necessary to state that our evidence is admittedly not so complete as we should like. A critical examination of the data shows us, however, that on the whole the influence of milk feeding on the metabolism of infants must be very slight. In certain instances the metabolism during quiet periods immediately after feeding is from 5 to 10 per cent. higher than eighteen to twenty-one hours after, while in others the metabolism twenty-one hours afterward, even in periods of complete muscular repose, was slightly greater than immediately after feeding. But the general picture derived from these observations indicates that the ingestion of milk played a very slight, if any, rôle in affecting the heat-production of the infants studied.

Recent observations in this laboratory during a thirty-one-day fast showed that as soon as food was completely withheld, the body storage of glycogen was rapidly drawn on and when exhausted, a distinct acidosis appeared. Our experience with diabetics and with normal persons subsisting on a carbohydrate-free diet⁵² gives evidence that such an acidosis tends to increase the basal metabolism. Additional light has been thrown on this subject by Schlossmann and Murschhauser,⁵³ who have shown in a recent publication the influence of the withdrawal of food on the excretion by infants of products of acidosis, particularly acetone, diacetic acid, and beta-oxybutyric acid. Even in the first hours of fasting, definite evidence of the excretion of beta-oxybutyric acid shows the beginning of acidosis. Knowing, as we do,

51. Schlossmann: *Atrophie und respiratorischer Stoffwechsel*, Kassowitz Festschrift, Berlin, 1912, p. 318.

52. Benedict and Joslin: *Carnegie Institution of Washington. Publication 176*, 1912, p. 134.

53. Schlossmann and Murschhauser: *Biochem. Ztschr.*, 1913, lvi, 396.

that acidosis strongly tends to increase the metabolism, one sees instantly that a point or a moment when the influence of the previously ingested food ceases and the influence of an oncoming, though slight, acidosis begins is extremely difficult, with our present knowledge, to foretell. It should not be overlooked, however, that Schlossmann and Murschhauser did not find an increased heat-production in these infants showing incipient acidosis although we are inclined to doubt the validity of drawing conclusions regarding so subtle a factor as acidosis from periods with such changes in the degree of repose.

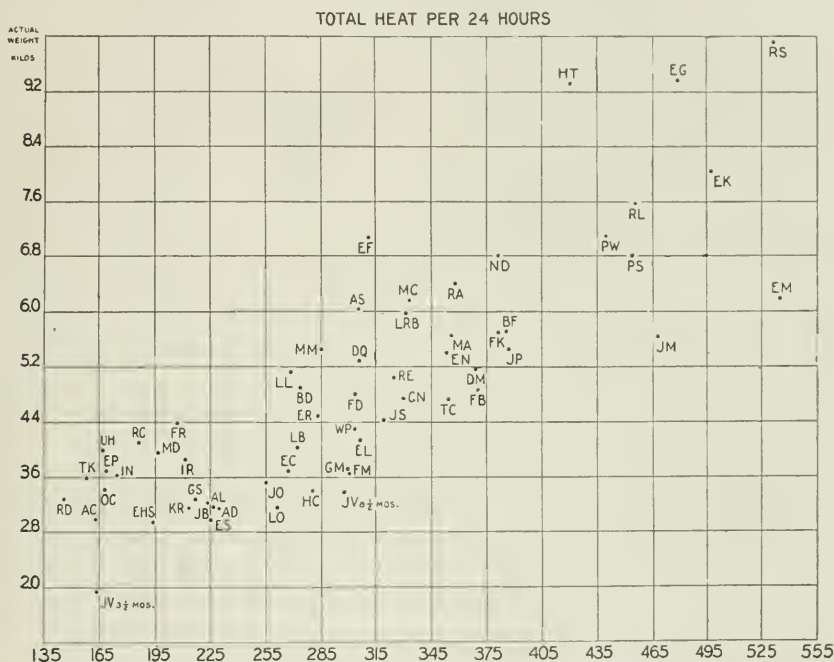


Fig. 9.—Chart showing the actual body-weight of infants and the total heat-production per twenty-four hours.

While, therefore, we recognize clearly that the presence of food in the alimentary tract of our infants has distinct theoretical objections, we believe that such influence, if it exists, can play no quantitative rôle in the striking comparisons of the basal metabolism of different infants which are made in the subsequent pages.

7. Comparison of Body-Weight and Metabolism

With the abundance of experimental material in hand, which was obtained with different infants, it is obvious that a large number of comparisons may be made in a variety of ways. Perhaps the simplest method of considering the results is on the basis of the total heat-

production. Accordingly a chart has been plotted showing the total heat-production of infants of varying weights, the actual weight at the time of the observation being used (Fig. 9). It is normally to be expected that a large animal gives off more heat than a small animal, and consequently we find that there is a tendency for the heavier infants to have a larger heat-production. Yet this is by no means invariably the case, for in a large number of instances, an infant of relatively small weight has a much larger heat-production than those of greater weight. Perhaps the most striking instance is

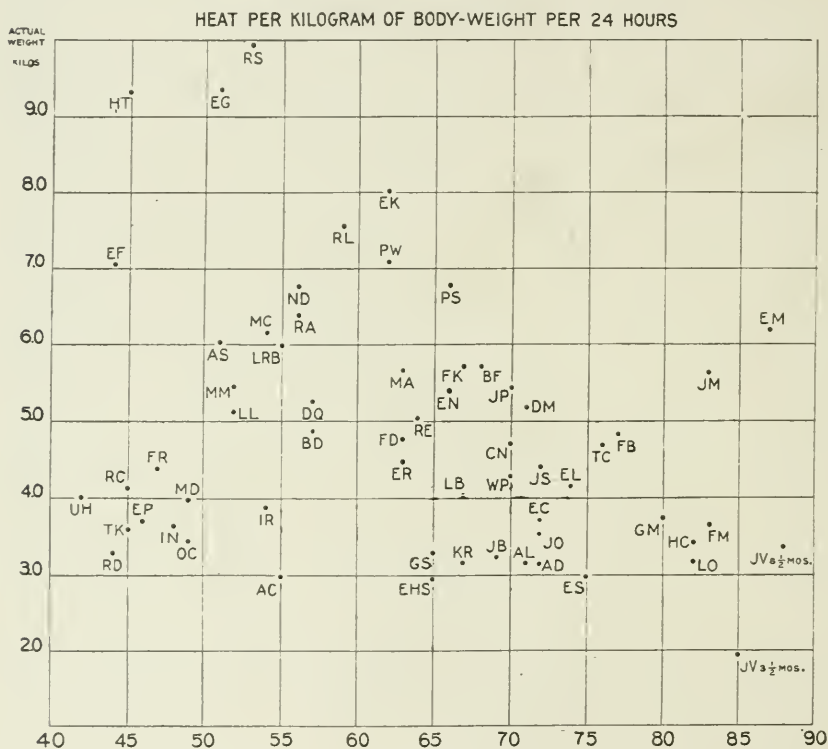


Fig. 10.—Chart showing the actual body-weight of infants and the heat-production per kilogram per twenty-four hours.

that with the subject E. M., who, with a body-weight of 6.2 kg., has 25 per cent. larger heat-production than has H. T. with a body-weight of 9.3 kg. While it is clear from the chart that in general the large infants show a larger heat-production, yet as there are many exceptions, no definite rule based solely on body-weight can be of great use. Although no general uniformity is seen at first in this curve, if one examine more particularly the values for the infants indicated as strictly normal in the table showing the clinical status of the infants

(Table 13), one can see that there is a distinct tendency to approximate a regular curve. Inasmuch as we are still occupied in overcoming the paucity of results obtained with normal infants, we hardly feel justified in laying sufficient stress on this point to designate specially the normals in our charts.

It has been the custom of many writers to compare the heat-production of persons of varying sizes by computing the heat-production per kilogram of body-weight, thus tacitly, at least, assuming a constancy in the heat-producing value of each kilogram of body-weight. Although dissenting from this principle, we have, for comparison purposes, computed the values for our infants on the basis of per kilogram of body-weight and give a part of them in Figure 10. Here there is, as would be expected, a large variation in the heat per kilogram of body-weight and no regularity is apparent. If the "normal" infants are selected, it is found that they, for the most part, lie under 65 calories per kilogram of body-weight, although they may go as low as 42 calories. For an intelligent comparison of the metabolism of different infants, therefore, it is evident that we have to deal with some factor or factors other than body-weight and no definite deduction can be drawn other than the fact that the majority of our "normal" infants have a heat-production per kilogram of body-weight somewhat under 65 calories per twenty-four hours.

8. Comparison of Body-Surface and Metabolism

For many years writers in metabolism have been wont to emphasize the significance of the relationship supposed to exist between the metabolism and the body-surface rather than that between the metabolism and the body-weight. The idea that there is an intimate relationship between body-surface and heat-production was first brought out by Bergmann⁵⁴ in 1847. The theory lay dormant for many years, but was finally resuscitated and put forth in a brilliant and highly stimulating manner by Rubner⁵⁵ in 1883, together with experimental evidence. Based fundamentally on Newton's law of cooling, it received great attention from practically all workers in physiology. The startling evidence which was brought forward to demonstrate that the heat-production per square meter of body-surface was about 1,000 calories for practically all species of animals lent further support to this hypothesis. In connection with our own researches we naturally expected to find a close relationship between body-surface and total metabolism, particularly in view of the fact that recent observations

54. Bergmann and Leuckart: *Anatomisch-physiol. Uebersicht des Tierreichs*, Stuttgart, 1852, p. 272. Bergmann: *Wärmeökonomie der Thiere*, Göttingen 1848, p. 9.

55. Rubner: *Ztschr. f. Biol.*, 1883, xix, 545.

from foreign laboratories appeared to confirm the validity of Rubner's law. We were, therefore, greatly surprised on preparing our final figures to find this intimate relationship entirely disturbed.

A. Methods Used for Measurement of Body-Surface

In order to discuss intelligently the relationship between the metabolism and body-surface, a critical examination of the various methods for determining the body-surface is essential. Using as a basis the relationship between the surface of similar solids which is expressed by the cube-root of the square of the weight, efforts have been made by a number of investigators to compute the body-surface of various animals and persons from the body-weight.

Meeh⁵⁶ found that he could measure the body-surface of men by using the constant 12.312, which, when multiplied by the cube-root of the square of the body-weight in grams, gave the body-surface in square centimeters. Rubner and Heubner,⁵⁷ who first applied this formula to the study of the total metabolism of infants, rightly substituted the value 11.9 which was determined by Meeh on two well-nourished infants under 1 year that he measured.

Recognizing the importance of taking into consideration the length of the body as well as the circumference of breast and abdomen, Miwa and Stoeltzner,⁵⁸ using Meeh's measurements, proposed another formula in which the length and circumference as well as weight should appear as factors. This formula has not been generally accepted by research workers.

Actual measurements of the body-surface of cadavers have also been used in an attempt to find some mathematical formula expressing the relationship between body-weight and body-surface. Lissauer⁵⁹ measured twelve cadavers, eleven of which were under 1 year, and found that the constant 10.3 should be used in the Meeh formula instead of those previously proposed. It has been maintained by other writers that since many of Lissauer's measurements were made on thin, poorly nourished, and atrophic infants, they do not give standards for well-nourished infants. Sytscheff⁶⁰ measured ten infants under 1 year of age, but computed no ratios. Howland,⁴³ employing Meeh's and Lissauer's measurements, has recently proposed still another method for computing the body-surface based on a curve represented by the algebraic formula $y = mx + b$.

56. Meeh: *Ztschr. f. Biol.*, 1879, xv, 425.

57. Rubner and Heubner: *Ztschr. f. exp. Pathol. u. Therap.*, 1904-1905, i, 1.

58. Miwa and Stoeltzner: *Ztschr. f. Biol.*, 1898, xxxvi, 314.

59. Lissauer: *Jahrb. f. Kinderh.*, 1902, lviii, 392.

60. Sytscheff: *Measure of Volume and Body-Surface of Children According to Their Ages*. Dissertation, St. Petersburg, 1902. See also Gundobin, loc. cit., p. 54.

With these three methods in vogue for computing the body-surface, that is, that of Rubner and Heubner using the Meeh formula with the constant 11.9; that of Lissauer using the constant 10.3 and that of Howland using the algebraic curve, it can be seen that with the great weight laid by all experimenters in infant metabolism on the relationship between body-surface and metabolism, it is incumbent on us to present our results on the three separate bases, although the relative values are unaltered in all three cases. This is done in Table 15.

B. Comparison of Actual Body-Weight and Heat-Production per Square Meter of Body-Surface

According to accepted ideas we should expect the heat-production per square meter of body-surface to be approximately constant for all of our infants. That this fact is far from being true is clearly

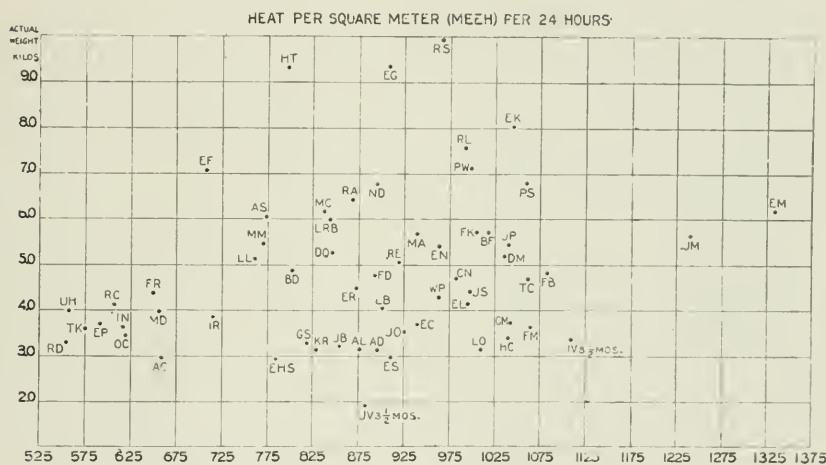


Fig. 11.—Chart showing actual body-weight of infants and heat-production per square meter of body-surface (Meeh formula) per twenty-four hours.

seen in Table 15, but the variations are most strikingly shown if we compare them with the actual body-weight of the infant, as is done in Figure 11. In this chart, which is made up on the Meeh formula, we should expect to find the values grouping themselves in a vertical line. On the contrary, the dispersion of the values is very noticeable, with a tendency, if any, toward a horizontal rather than a vertical alignment. An actual variation from 554 to 1,334 calories or 140 per cent. is recorded. Omitting the extreme cases, J. M. and E. M., although frankly we see no reason why they should be omitted in this comparison, the range is 554 to 1,108 or 100 per cent. Even "normal"

infants range from 554 to 998 calories. Thus the complete absence of correlation between weight and the heat-production per square meter of body-surface is strikingly shown. It is again important at this point to recall the fact that the observations made on these infants were all under constant conditions, namely, complete muscular repose and approximately the same length of time after feeding. It is impossible, therefore, to explain these great discrepancies as due to muscular activity, nor can they in any way be accounted for by the ingestion of food, as our experiments have shown that the food taken by these infants while under observation has no material influence on the metabolism. Although we are deferring its discussion until a later article, it is of interest to point out here the low heat-production per square meter of the numerous new-born infants.

9. Effect on Metabolism of Possible Disturbance in Relationship Between Body-Surface and Body-Weight

It has frequently been the custom when discrepancies in the heat-production per square meter of body-surface are found with infants, and particularly with atrophic infants, to ascribe the variation to a disturbance of the relationship between body-surface and the body-weight from which it is computed. It is essential, therefore, at this point to discuss this possibility more in detail.

The argument frequently raised is that disturbances in the relationship between body-weight and body-surface with underweight infants precludes the use of any of the formulas now regularly used for the computing of body-surface, in that they give too small a value of body-surface for such infants. At the outset we wish to oppose this general thesis on the ground that in the most extensive and remarkably accurate series of measurements on infants with which we are familiar, namely, those of Lissauer, it is especially emphasized that ten out of twelve of the infants were very much under weight. This will be seen by reference to Table 16, which reproduces the weights of eleven of the infants measured by this investigator.⁵⁹

As Lissauer himself points out with regret, S-i was the only infant that could be called normal, although S-r was practically of normal weight. All of the other infants were noticeably under weight, far more so than our infants as a rule. Yet, in spite of this great deficiency in weight, the relationship between the body-weight and the measured body-surface was represented by the difference between the constant 10.3 used by Lissauer and 11.9, the constant of Meeh. In other words, this large variation in weight produced a maximum discrepancy of not over 15 per cent. in the relationship between the body-surface as actually measured and the body-weight.

We believe that Lissauer's formula, in general, more nearly fits the requirements of observations in clinics, where the larger number of infants are under weight. On the other hand, as we have already pointed out, it is distinctly questionable whether the methods of measurement⁶¹ have even yet been sufficiently refined or are sufficiently numerous to give a reliable method for the computation of the body-surface from the body-weight.

Although we believe that the lack of consistency exhibited by our infants in the heat-production per square meter of body-surface may not be ascribed to the fact that these infants were distinctly under the

TABLE 16.—BODY-WEIGHTS OF INFANTS MEASURED FOR BODY-SURFACE BY LISSAUER

Name	Sex	Age	Body-Weight, kg.	Average Weight for Age Obtained from Heubner, kg.
M-f.....	M	3½ months	3.27	6.2
H-r.....	F	3½ months	1.96	6.2
R-e.....	F	3¾ months	3.37	6.3
S-e.....	M	1 month	2.22	4.008
S-r.....	F	1 month	3.83	4.008
M-r.....	M	15 months	5.23	11.+
W-t.....	M	17 days	1.73	3.6
S-t.....	M	22 days	1.28	3.7
P-z.....	M	3¼ months	2.50	6.0
H-z.....	M	7½ months	3.10	8.2
S-i.....	M	3¾ months	6.18	6.3

average weight, it is of special interest to select a few infants who are of normal average weight and note the relationship between the heat-production and the body-surface. This has been done in Table 17, in which the heat-production per square meter has been calculated for eight of our normal infants of average weight.

61. As an interesting evidence of our initial belief in the importance and significance of the measurement of body-surface and its relationship to metabolism, we should here state that extensive preparations were made by us for the measurement of the body-surface of a number of infants, and a method was developed for securing shadow photographs of infants in various positions, the areas of the shadows being measured by a planimeter. It was our hope to establish thereby some relationship with the body-surface as measured from the shadow photograph, and by actual measurements of cadavers, and the body-weight and length. It is needless to say that with our present views in regard to the significance of body-surface in the relation to metabolism we have not felt justified in continuing such a series of measurements.

10. Influence of Variations in the Composition of the Body on Total Heat-Production

Since a gross disturbance in the relationship between the body-weight and the body-surface as computed from the body-weight is highly improbable whether the infant is atrophic or well-nourished, it is important to find out, if possible, if any relationship exists between the general composition of the body and the total heat-production. Our data are sufficiently extended to permit a somewhat incomplete discussion of this important phase of the comparisons.

Heretofore, all workers in metabolism have considered only the relationship between body-weight and metabolism, or body-surface and metabolism. Since the body-surface is assumed to have a direct relationship to the body-weight, it can be seen that body-weight is

TABLE 17.—HEAT-PRODUCTION PER SQUARE METER OF BODY-SURFACE (MEEH FORMULA) FOR NORMAL INFANTS

Subject	Body-Weight Without Clothing kg.	Height cm.	Age	Experi- mental Days	Periods	Heat per Square Meter of Body- Surface (Meeh) cals.
M. D.	3.99	..	17 days	2	4	656
L. L.	5.13	57	2½ mos.	10	13	759
B. D.	4.90	58	2 mos.	2	4	802
M. C.	6.17	63	4 mos.	3	7	837
L. R. B. ..	5.99	64	4 mos.	4	11	844
E. G.	9.37	74	10 mos.	3	5	907
R. L.	7.58	71	8½ mos.	5	8	991
P. W.	7.11	64 ?	7 mos.	2	5	998

the only fundamental factor which has thus far been seriously considered by investigators in comparing the metabolism of different infants.

It is obvious that when two infants are of the same weight, the shorter one will have the larger proportion of fat. Furthermore, with two infants of the same length but of different weights, the heavier infant will have the larger proportion of fat. It can be seen, therefore, than an atrophic infant, weighing 4 kg. and 65 cm. long, when compared to a well-nourished infant of the same weight and length, would have a smaller proportion of fat. Moreover, an atrophic infant, to have the same weight and length as a normal infant, must obviously be older, and we here find a new factor entering into the comparison of infants; as yet the element of age has received scant attention.

An inspection of Table 15 will show that in a number of instances infants with approximately the same body-weight and the same height differ greatly in age. Unfortunately our data are not so extensive as to enable us to compare infants with absolutely the same body-weight and height, but a number of comparisons are justifiable and these have been included in Table 18.

In this table eight series of comparisons are made of the total heat produced, the heat-production per kilogram of body-weight, and the heat-production per square meter of body-surface for infants with

TABLE 18.—COMPARISON OF HEAT-PRODUCTION OF INFANTS OF LIKE BODY-WEIGHT AND HEIGHT, BUT OF DIFFERENT AGES

Subject	Sex	Body-Weight kg.	Height cm.	Age mos.	Heat Produced		
					Per 24 Hours cals.	Per Kilogram per 24 Hrs. cals.	Per Sq. Meter (Meeh) per 24 Hrs., cals.
A. L.....	F.	3.18	53	4	226	71	876
J. V.....	F.	3.38	53	8½	297	88	1,108
E. N.....	F.	5.40	66	6	353	66	962
D. M.....	M.	5.18	66	11	369	71	1,034
M. M.....	F.	5.47	62	4½	285	52	770
J. M.....	M.	5.63	62	8	467	83	1,239
D. Q.....	M.	5.28	62	4½	305	57	846
J. P.....	M.	5.45	63	7	387	70	1,039
M. M.....	F.	5.47	62	4½	285	52	770
J. P.....	M.	5.45	63	7	387	70	1,039
D. Q.....	M.	5.28	62	4½	305	57	846
J. M.....	M.	5.63	62	8	467	83	1,239
L. R. B....	F.	5.99	64	4	331	55	844
F. K.....	M.	5.71	65	7	381	67	1,003
H. T.....	M.	9.33	75 ?	5½	420	45	797
E. G.....	M.	9.37	74	10	479	51	907

the same body-weight and height but of different ages. The difficulties incidental to measuring exactly the length of infants make these measurements slightly problematical and there may be a variation of plus or minus 1 cm. We have, therefore, compared infants whose lengths do not vary more than 1 cm. The variations in weight are all within a few tenths of a kilogram.

We note instantly several striking points in the data as presented. In each comparison the values for the younger infant are given first.

and it will be seen that the older infant has invariably the larger total heat-production. The greatest difference is 182 calories in the comparison of M. M. with J. M., the lowest difference being that of 16 calories between E. N. and D. M. Aside from this latter comparison, the increase in the heat-production for the older infants is very considerable. The heat-production per kilogram of body-weight and per square meter of body-surface also shows this increase in the same general proportion since the body-weights of the infants compared are essentially the same in all cases.

In the two series of comparisons in which the youngest infant is approximately 6 months old, namely, those comparing E. N. with D. M. and H. T. with E. G., the increase in the heat-production for the older infant is not so great. In the latter comparison, E. G. was of normal weight while H. T. was over weight so that the excessive amount of fat actually lowered the total heat-production of the younger infant H. T. It is therefore clear that with the older infants, which were in most instances distinctly under weight, there was a deficiency in the fat with an accompanying increase in the proportion of active protoplasmic tissue. While this method of comparing the metabolism of infants on the basis of weight, height and age gives a clue to the probable preponderance of fat or active protoplasmic tissue, it is obvious that no quantitative relationship can be established on this basis.

The striking comparison between M. M. and J. M. is particularly worthy of consideration, inasmuch as the value for M. M. is derived from observations on three days, and a total of seven satisfactory periods were available for averaging, while with J. M. the data were secured on two days with six periods for comparison. Here, with a difference of $3\frac{1}{2}$ months in the age, there was obviously a much greater proportion of active protoplasmic tissue with the older infant, J. M.

That the active protoplasmic tissue determined to a very considerable extent the total catabolism, not only with J. M., but with all of the older undernourished infants, is highly probable and we find ourselves thoroughly convinced that the metabolism is determined not by the body-surface but by the active mass of protoplasmic tissue. With normal infants of varying weights, it is quite probable that the active mass of protoplasmic tissue varies directly with the age. Since it has been shown that not only body-surface but also more recently the blood-volume, the size of the aorta, and the size of the trachea with several species of mammals bear a direct relationship to the cube root of the square of the body-weight,⁶² it is not surprising that most

62. Dreyer and Ray: *Phil. Tr.*, 1909-1910, cci, ser. B, 133; Dreyer, Ray and Walker: *Proc. Roy. Soc.*, London, 1912-1913, lxxxvi, ser. B, 39 and 56.

experimenters have observed that with adults the metabolism is roughly proportional to the body-surface. If the blood-volume and the area of the trachea and the aorta are proportional to the cube root of the square of the body-weight, it is reasonable to suppose that the active mass of protoplasmic tissue may develop normally on this ratio. When there are marked variations from the average, as with excessive or with deficient adipose tissue, this relationship cannot be expected to hold.

If, therefore, it is maintained that the total metabolism is proportional to the body-surface, it should be stated that this is not due to the fact that there is a loss of heat from the body-surface and that Newton's law of cooling determines the intensity of the metabolism, but that with normal persons the body-surface, blood-volume, the area of the trachea and aorta, and probably the active mass of protoplasmic tissue, are all in simple mathematical relation to the body-weight. Thus the apparent relationship which has previously been observed between the heat-output and the body-surface with normal or nearly normal persons has an explanation in that with such persons a simple relation exists between the body-surface, blood-volume, body-weight, and the mass of active protoplasmic tissue.

In our series of observations we have attempted to eliminate completely all muscular activity, to make the experiments under approximately the same conditions as to nutriment, to select such a diet as was least stimulating to the catabolism and to have our subject for the most part in deep sleep, thus eliminating psychic disturbances. With these conditions we hoped to obtain the fundamental minimum metabolism, on which we might base our discussion.

The basal metabolism as we have outlined above, cannot in any wise be considered a direct function of the body-weight and the body-surface and particularly has no relationship with body-surface on the basis of the law of cooling bodies.

We believe that our evidence points strongly and conclusively to the fact that the active mass of protoplasmic tissue determines the fundamental metabolism. The absence as yet of a direct mathematical measure of the proportion of active protoplasmic tissue does not, we believe, in any wise affect the convincing nature of our evidence.

A CASE OF ACUTE CHYLOUS ASCITES (NON-FATTY,
PSEUDOCHYLOUS, LACTESCENT OR MILKY
TYPE) IN A BOY EIGHT YEARS OLD *

FRANCIS HUBER, M.D.
NEW YORK

OPERATIONS AND SURGICAL COMMENTS BY
HENRY M. SILVER, M.D.
NEW YORK

In a recent most valuable, thoroughly scientific and exhaustive monograph Dr. S. Gandin of St. Petersburg, discusses the different types of chylous effusions in serous cavities. The work is based on the study of three medical and two surgical cases, and a critical review of 281 references covering the literature up to date.

The classification chylous, chyloform and milky, non-fatty forms of ascites, is not universally adopted. Many of the more recent writers make no distinction between the chylous and chyloform varieties; others prefer to retain the designation chyloform (which does not necessarily refer to the origin of the fluid), some again do not make any distinction between the fatty and the non-fatty ascites, regarding them, in contradistinction to the chylous, as chyloform or pseudo-chylous.

This confusion has led to a further distinction of mixed types, chylous-adipose, chylous-pseudochylous and adipose pseudochylous effusions.

1. The *true chylous* is due to the presence of chyle. 2. The *chyloform or fatty*, though resembling the first, owes its milky-like appearance to emulsified fat, the result of a fatty degeneration of cellular elements. 3. Finally, in the third variety, the opalescence is not due to the presence of fatty emulsion, but is caused by some opalescent substance, the exact nature of which is still undiscovered.

Chylous ascites is due to the escape of chyle from the duct or receptaculum chyli, the result of trauma or disease processes, malignant or benign. The specific gravity varies from 1.007 to 1.033, average 1.0158. The reaction is alkaline or neutral.

The fluid resists putrefaction, is without odor, does not clot, but may separate into layers on standing, the fat appearing on top. This variety is distinguished, first, by the finely divided state of the fat, and

* Read by title at meeting of the American Pediatric Society, May, 1914.

secondly, by the absence of leukocytes or other cells showing fatty changes.

The chylous and chyloform effusions have been carefully studied, not only as to their composition, but also from the pathological standpoint. Wallis and Scholberg (1910) believe that there are no characteristic pathological anatomical changes.

Kelly (1907) would restrict the name to cases in which injuries or ulcerations of the chylous system have been found.

Witlin (1909) believes that chylous ascites or chylothorax can only be explained by trauma.

Between these extremes there are those who would explain the occurrence by stasis or evidence of pressure on the thoracic duct; others find macroscopic changes somewhere in the chylous system; finally some base their diagnosis on microscopic changes in the vessels, or on the grounds of an individual anatomical predisposition.

Undoubted cases of a rupture (trauma or result of disease processes) in some portion of the chylous system, have been reported as of occasional occurrence.

Mechanical obstructions in any part of the course of the duct from the receptaculum chyli to the left subclavian vein, or in some of the tributaries in the mesentery, the result of cicatricial contractions, new growths, cysts or tumors, may give rise to stasis and transudation through the weakened and dilated walls. In some of these cases diffuse dilatations of the main duct or entire chylous system were found¹; in others more or less localized distention of the vessels in the mesentery and intestinal walls existed, depending on the situation of this obstruction. It must be remembered that pathological conditions which lead to a gradual interference in the ductus are more readily compensated through the collateral circulation than those of acute origin, a circumstance which may explain the rarity of cases.

Chyloform or fatty (adipose) ascites differs from the above. It is not due to leakage of chyle but to the formation of fat in the effusion; the globules are larger and cells containing fat are present, specific gravity 1.009 to 1.026; average, 1.01625. It is usually associated with intra-abdominal new growths or with chronic peritonitis, simple or tuberculous.

The origin of the fatty, lactescent type, has been attributed to fatty degeneration of cellular elements, a lipemia, etc.

The non-fatty, pseudochylous, lactescent or milky type is differentiated, as the name implies, by the absence of fat. Specific gravity 1.005 to 1.030; average, 1.0132.

1. Such an effusion does not lose its milky appearance after being shaken up with ether, benzol, chloroform, etc., even though rendered alkaline beforehand.

2. When fat is present the amount is too small to give rise to a milky appearance.

3. The microchemical reactions of fat (specific color, effects of heat and fat solvents) are negative.

4. Precipitation of the albumen leaves a clear solution.

5. Finally in a number of cases the opalescence is presumed to be due to minute particles of albumen, nucleo albumen, mucoid, lecithin, lecithoglobulin, etc. Gandin,¹ who has carefully reviewed the voluminous literature and weighed the evidence, does not believe that the negative results of the microchemical reaction of the so-called pseudochylous fluid invalidate the assumption of the fatty nature of suspended molecular granules.

In considering critically and at length the various properties (physical, microscopic, chemical, and physiological) of chylous, chyliform and pseudochylous fluids, Gandin¹ is unable to establish any important differential characteristics; furthermore, he does not think that we are justified in the use of the above-mentioned classification. A thorough critical review of the pathogenesis of the chylous and pseudochylous types leads to a similar result. His conclusions based on his studies and experiments, are briefly as follows:

GANDIN'S CONCLUSIONS

1. The addition of even small percentages (0.01 to 0.1 per cent.) of the finely emulsified fat of chyme or homogeneous milk to a transparent fluid gives rise to a milky cloudiness.

2. The milky appearance of an effusion in a serous sac is due to the presence of emulsified fat.

3. It has not been demonstrated in a satisfactory manner, that the presence of any substance excepting emulsified fat, can give rise to the milky appearance. The presence of emulsified fat in milky effusions, without the admixture of chyle is not probable, nor has such been demonstrated.

4. As chyle represents the only recognized source of finely emulsified fat in the body, milky and opalescent effusions must be regarded as chylous.

5. The terms "chyliform" and "pseudochylous" are not applicable as distinct pathogenetic entities, consequently they are superfluous.

6. Effusions, containing fat in drops, but not in an emulsified form, do not present the typical milky appearance.

The term fatty (adipose), introduced by Quincke, is applicable to such cases.

1. Gandin, S.: *Pathogenese und Klassifikation der Milchartigen Ergüsse*, *Ergebn. d. inn. Med. u. Kinderh.*, 1913, xii, 219.

CASE REPORT

History.—S. H., male, aged 8, was admitted to Beth Israel Hospital Dec. 15, 1913. He was born in New York and had never been in any of the southern or eastern countries.

The family history has no bearing on the case. He had measles when 7 months old, and what was supposed to have been a nephritis, with edema of the extremities, clearing up after four weeks illness, at age of 4 years. With the exception of pneumonia at 5½ years, the boy was reported to have enjoyed fair health up to the time of his present illness.

Careful questioning failed to elicit any history of trauma. Two weeks before admission the child felt generally ill, suffering from a severe nasal discharge, though he continued to attend school. A week later he vomited undigested food, since which time his appetite has been poor. Two days before he entered the hospital the father on dressing the child noticed an increase in the size of the abdomen and a swelling of the genitals. No fever, cough, headache, general weakness or urinary disturbances were present.

Physical Findings.—The patient was fairly well developed, somewhat anemic and rather poorly nourished. No evidences of prostration, dyspnea, no petechia or other eruption or glandular enlargement were noticed.

Heart and lungs negative. Abdomen symmetrically enlarged, fluctuation wave readily transmitted from side to side. Careful palpation failed to reveal a tumor or any swelling in the abdominal cavity; no tenderness or rigidity present. The veins were markedly distended over the lower half of the abdomen and right upper quadrant; also over the upper parts of both thighs. The center of the abdomen was tympanitic; the flatness in the flanks, changing quickly with a change in the position of the patient, showed a large amount of free fluid in the abdominal cavity.

The edema of the penis and scrotum was quite marked. There was slight edema of the thighs, but none about the feet or ankles; abdominal walls and back slightly infiltrated. The temperature was 100 F. It quickly fell to normal and remained so. The pulse, which was 120, rapidly came down to 80, varying between 80 and 100; at times 110. The respirations were 24 to 30. Red blood-cells, 4,700,000; hemoglobin, 70 per cent.; white blood-cells, 9,800; lymphocytes, 16 per cent.; polynuclears, 79 per cent.; eosinophils, 4 per cent.; mastcells, 1 per cent; urine negative. Von Pirquet negative on repeated occasions. Wasserman also negative.

Two weeks later red blood-cells, 3,500,000; hemoglobin, 65 per cent.; white blood-cells, 10,000; lymphocytes, 11 per cent; polynuclears, 88 per cent.; eosinophils, 1 per cent. Phenolsulphonephthalein test for renal efficiency 30 per cent. on one occasion and 20 per cent. the second.

Though the general condition remained excellent, appetite "simply enormous" with regular bowels, the abdomen became larger, the diaphragm being pushed up as high as the middle of the scapula on the right side, and lower angle on the left. Edema of the genitals and thighs, particularly the left, also increased; the subcutaneous tissues of back and abdominal walls pitted on pressure. Notwithstanding distention there was relative little discomfort or dyspnea. The urinary excretion was greatly diminished, about 8 or 9 ounces daily, though allowed at least 20 ounces of fluids. Urine negative, no casts, cells or bacteria.

Management.—Jan. 6, 1914, the abdomen was tapped in customary manner; over 3,000 c.c. of a slightly turbid, milky fluid were removed to relieve the distention. A considerable amount, approximately half, was allowed to remain. Microscopically a few lymphocytes and some finely granular matter with brownian movements were found. Evaporating a drop on the slide, crystals of sodium chlorid were detected. A bacteriological examination failed to reveal any organisms. No sugar or fat present.

EXAMINATION OF ASCITIC FLUID

From S. H.

Quantity about 500 c.c.; color and appearance, milky, still turbid after filtration; specific gravity, 1.011 (20 C.); reaction, neutral; total solids, 1.25 per cent.; material in suspension, 0.016 per cent.; ash, 0.72 per cent.; organic matter, 0.53 per cent.; sodium chlorid, 0.64 per cent.; sulphates, *nil*; urea, *nil*; sugar, *nil*; albumin, 0.319 per cent.; primary proteose, 0.055 per cent.; secondary, also present, unestimated; globulins (indications ?) not estimated; fats, absent.

LOUIS E. SALAS, M.A., B.Sc.

For four or five days subsequently, considerable oozing took place through the small puncture, necessitating a change of dressing several times daily. The edema of the scrotum and abdominal walls diminished. As soon as the slight wound had healed, the abdomen refilled rapidly and the edema of the back, abdomen and thighs also increased, necessitating a second tapping. January 17 over 2,000 c.c. were taken away. It presented the same opalescent appearance, similar to that removed before. The rapid recurrence of the ascites, it seemed to us, demanded more radical measures. If the abdominal fluid, rich in proteins, salts, and the characteristic constituents of the tissues and body fluids could be diverted to the blood and lymph streams, the patient certainly would gain in every way. After a consultation with my surgical colleague, Dr. H. M. Silver, an exploratory laparotomy was decided on, first, with a view to a clearing up the nature of the lesion, and secondly, to determine the possibility of draining the "peritoneal pond" into the subcutaneous tissues of the thighs and abdominal walls. This part of the subject will be taken up by Dr. Silver to whom my sincere thanks are tendered for his interest and skilled surgical aid in the care of this interesting case.

Diagnosis.—A careful consideration of the physical condition and the history of our patient did not enable us to hazard any suspicion as to the etiology. In the absence of any traumatism, the rapid appearance of ascites, the large prominent veins with local edema of abdomen and genitals, pointed to some intra-abdominal pressure, though no tumor or other swelling could be detected, even after tapping. The general appearance and bearing of the child were against malignancy.

The character of the fluid obtained by tapping, its milky opalescent hue, and the absence of cells filled with fat, justifies a diagnosis of chylous ascites (third variety), non-traumatic in nature and of uncertain origin.

DISCUSSION

A majority of the writers believe that the chylous origin of the fluid may be established or recognized clinically, first, by the "test of Strauss"; secondly, by the rapid return of the fluid after tapping.

The Strauss test is based on the fact that the amount of fat in the chyle depends on the diet. Thus, if a larger amount of fat is allowed or a smaller percentage is taken in, corresponding changes will be noticed in the fat contents of the fluid removed in repeated tapings at regular intervals. Though confirmed by some, the results obtained by other observers have been rather conflicting.

The rapid accumulation of the fluid noted in our case and in others reported in literature, has been the subject of comment by many authorities.

It was observed by Vermage in 1700, and confirmed by many writers subsequently.

Senator attributes the rapid recurrence to stasis, either in the portal system or in the chyle-duct or lymphatic circulation. Others conclude that there has been a rupture of some portion of the duct or one of the tributaries, permitting the escape of chyle into one or other of the serous cavities. On the other hand, instances have been recorded in which the fluid did not return quickly. And furthermore we should not forget that in other pathological states, as advanced cases of cirrhosis of the liver, in which the question of chylous ascites does not enter, a rapid return of the fluid is not unusual.

Aside from the presence of the chylous fluid, the case is interesting in many other respects. For instance:

1. The small amount of urine passed. Though only 8 or 9 ounces were excreted in twenty-four hours, there was no evidence of any systemic disturbances, as headache, nausea, vomiting, etc.
2. The general well being of the patient. Excepting the discomfort due to the distended abdomen, the boy did not make any complaint. The appetite was good and bowels regular. Pulse and temperature normal.
3. The rather unusual type of ascites with edema of the back, abdomen, thighs and genitals (ankles, legs and chest, not involved) and no edema of the face at any time throughout the course of the disease.
4. The rapid return of the fluid after tapping, presumably explained by the fact that a collateral circulation had not been established, as condition was rather acute.
5. The marked diminution in the amount of edema of abdomen, genitals, etc., after the tapping, and its rapid return when the puncture had healed.
6. The rapid subsidence of the external localized edema after operation.
7. The decided increase in the urinary excretion soon after operation, evidently the direct results of the removal of the intra-abdominal pressure and the establishment of peritoneal drainage.
8. The brilliant success of the surgical measure adopted.

OPERATION WITH SURGICAL NOTES

HENRY MANN SILVER, M.D.

Early in January of this year (1914) Dr. F. Huber requested me to see and operate on a boy 8 years old, suffering from chylous ascites. As a careful history of the case has been given above, it will not be necessary to repeat it. Although the patient was in rather poor condition, and the fact was recognized that ascites patients have an impaired vital resistance, deficient powers of repair, and do not stand

well extensive operations under general anesthesia, it was decided to do an exploratory laparotomy as quickly as possible under ether anesthesia.

Exploratory Laparotomy.—An incision beginning just below the umbilicus and extending downwards for 3 inches just to the right of the median line was made through the layers of the abdominal wall. When the peritoneum was opened considerable fluid escaped and about 1,500 c.c. were drawn off by the aid of the suction apparatus.

The coils of small intestines presenting in the wound were greatly distended with gas and very pale, and on careful examination of all the coils within reach a most interesting condition was observed. The lacteal vessels, not only on the intestines, but in the mesentery, were much enlarged, being flexuous in their course, constricted at intervals and presenting a beaded or varicose appearance. The constrictions on the intestines were so tight in places that the lacteal vessels would disappear only to reappear in the mesentery. Enlarged glands were found in the mesentery, small near the intestines, but growing larger as they passed to the root of the mesentery where they became very numerous. Some were about the size of a small hickory nut, soft, elastic and of a yellowish color. It was not deemed advisable to remove one for the purpose of closer study and microscopic examination, as the child's condition was not good. As careful an examination was made of the organs within the abdominal cavity as was possible through a 3-inch incision. Nothing abnormal was detected. Before closing the wound, the question of what form of drainage should be resorted to, presented itself.

The ascites was chylous, came on quietly, the child had not been living with any tuberculous patient at home, gave no history of injury, and there were no evidences of compression of the portal vein, as the intestines and omentum were pale and showed no sign of congestion. As it seemed to me that the ascites was due to compression and distention of the lymphatic or chylous vessels by the large number of enlarged glands within the mesentery, some simple form of internal drainage which could be quickly done was called for. This would relieve the intra-abdominal pressure until the child's general condition could be improved by good food, fresh air, sunlight and possibly some form of medication. Moreover, it would conserve a fluid rich in proteins, salts and the characteristic constituents of the body fluids; the little boy had already lost over 5,000 c.c. of this fluid withdrawn at two previous tapings.

The internal drainage was carried out as follows: Six strands of No. 7 white silk 4 inches long were caught in the grasp of a narrow-bladed dressing forceps, carried into the abdomen and thrust through the peritoneum to the outer side of the femoral vessels into subcutaneous tissues of the thigh, only half an inch of the silk remaining within the peritoneal cavity. This was repeated on the opposite side. At the upper angle of the wound six more strands of silk of the same length as used below were thrust into the subcutaneous tissues of the abdominal wall above the umbilicus, the lower half inch remaining within the abdominal cavity. Great care was taken to allow only a very little of the silk to project within the abdominal cavity, as it has been found by actual experiment that long silk strands may cause intestinal obstruction by forming attachments to the omentum or any organ within reach.

Course.—The patient reacted well and his convalescence was rapid and uneventful. The dressings were removed at the end of a week and the wound was found completely healed, with no edema of its edges. There was some edema in the upper part of the right thigh, very little in the left thigh, and none over the upper portion of the abdomen. The patient was allowed to be up and about the ward early in order to maintain the circulation of the body fluids by exercise, especially in the portal and lymphatic systems. The boy was discharged from the hospital in fine condition the latter part of March.

No evidences of fluid within the abdomen could be found; there was no edema of the thighs or abdominal wall; no thickening of or about the silk drains could be felt.

Five months after operation the boy was found to be in excellent health; the fluid had not returned. Abdomen lax, no masses could be felt on a most careful examination, nor could any thickening be made out in the neighborhood of the silk drains.

Although Lambotte² of Antwerp, was the first to use silk to drain the abdomen, it was not until Mr. W. Sampson Handley³ published his work on the use of silk for artificial lymphatics in cases of brawny arm in the last stages of breast cancer, also its use in draining fluid from the abdominal cavity, that surgeons began to give this method of drainage any attention. Handley from an experience gained from an interesting case of ascites which showed but little edema of thighs and upper abdominal wall after operation, draws the following inferences:

(1) Without causing edema, drainage into the thigh has gone on since the operation; (2) if the absorptive powers of the tissues are normal, and the amount of fluid led into them is not excessive, the appearance of edema is not to be expected.

McDill⁴ in order to determine the exact changes that took place in the silk used for abdominal drainage carried on a number of experiments in animals. He found that the short intra-abdominal ends showed a densely organized membrane of connective tissue outside of the silk and a general infiltration of the meshes by cells, single, in bundles, and in septa; although the angle of the silk with the peritoneum is plainly marked, showing an actual ectropium of the peritoneum along side of the silk which really acts as a silk connective tissue plug. This angle is the place at which McDill claims that an intraperitoneal fluid must find its exit by pressure and gravity to the subcutaneous lymph spaces, along the outside of and not within the body of the silk.

2. Lambotte, E.: *Semaine méd.*, 1905, xxv, 19.

3. Handley, W. S.: *Brit. Med. Jour.*, April 16, 1910, p. 925.

4. McDill, J. R.: *Surg., Gynec. and Obst.*, Nov., 1913, p. 523.

PROGRESS IN PEDIATRICS

REVIEW OF THE LITERATURE ON THE FEEDING AND GASTRO-INTESTINAL DISEASES OF INFANTS, FOR THE YEAR 1913-1914

GRACE MEIGS, M.D.

CHICAGO

BREAST-FEEDING

1. Kleinschmidt: *Monatschr. f. Kinderh.*, 1913, xii, 423.
2. Czerny: *Med. Klin.*, 1913, ix, 895.
3. Langstein: *Ztschr. f. Kinderh.*, 1913, vii, 193.
4. Ritter: (Abstr.) *Jahrb. f. Kinderh.*, 1913, lxxviii, 613.
5. Frost: *Arch. Pediat.*, 1913, xxx, 608.
6. Reuben: *Arch. Pediat.*, 1914, xxxi, 176.
7. Bamberg: *Ztschr. f. Kinderh.*, 1913, vi, 424.
8. Langstein: *Jahreskurs. f. Aerzt. Fortbild.*, 1912, iii, No. 6.
9. Koller: *Cor.-Bl. f. schweiz. Aerzte*, 1912, xlii, 777.
10. Rosenstern: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 1834.
11. Jones: *Arch. Pediat.*, 1914, xxxi, 24.
12. Hoobler: *Arch. Pediat.*, 1914, xxxi, 171.
13. Talbot: *Boston Med. and Surg. Jour.*, 1913, clxix, 760.
14. Lee: *Arch. Pediat.*, 1913, xxx, 509.
15. Engel: *Monatsch. f. Kinderh.*, 1913, xii, 559.
16. Heydolph: *Jahrb. f. Kinderh.*, 1913, lxxviii, 216.

In all recent publications on infant-feeding the superiority of breast-milk over all artificial foods is more than ever emphasized; and the crusade for the encouragement of breast-feeding continues. The cause of this undoubted superiority is still an unsolved problem. One especial phase of the subject which is greatly discussed is the far greater immunity to infection shown by breast-fed infants. This is emphasized by Kleinschmidt,¹ Czerny,² Langstein,³ Meyer and others. They have shown that all methods of artificial feeding, however successful in other respects, give no immunity against infectious processes. What is the essential cause of the high immunity conferred by breast-milk? The passage of immune bodies from mother to infant in the mother's milk has long been considered a possibility. Czerny² believes that this has not been proved; but believes the cause lies rather in the high fat content of breast-milk. Langstein³ advises feeding all infants who are much exposed to infection on breast-milk.

A theory advocated for some time by German authors is that there is shown but little variation in the breast-milk of different women, or in the same woman under different conditions; that all breast-milk is

good. Langstein says that differences in breast-milk have not been proved; that until they are he will adhere to the idea that all breast-milk is adapted to the child.

Bamberg⁷ studied the composition of the milk of wet-nurses giving very large amounts of milk; also of a few during menstruation. He found no change in the constituents under these two conditions.

Heydolph¹⁶ saw no bad effects in infants after continuance of breast-feeding during mastitis, even though there was pus in the milk.

Ritter,⁴ on the other hand, believes that all breast-milk is not alike, and that the wide variations in fat should be studied. Frost⁵ believes that nervous shock in the mother may cause changes in the breast-milk harmful to the infant, and that under such circumstances all the constituents of the milk may be changed.

Reuben,⁶ in a large experience at milk stations, finds that the breast-milk of most of the women deteriorates or becomes insufficient after the seventh or eighth month; and that the children weaned altogether at that time thrive much better than those given "*allaite ment mixte*." Langstein, too, on the ground that after the ninth month the breast-milk contains too little iron, advises weaning and the giving of a small amount of vegetable purée, besides the feedings of milk dilutions.

Jones¹¹ has reviewed the recent statistics as to the ability of mothers to nurse their infants.

Most authors seem agreed that the only stimulus for milk secretion is the normal one of the sucking of the infant; so that in the event of a delayed or insufficient milk secretion, waiting, with a systematic putting of the infant to the breast, are indicated.

Koller⁹ disagrees; he believes that milk secretion is not merely passive, caused by suction on the nipple, but active, depending on the nervous condition of the mother. Rosenstern¹⁰ has shown that in many cases of apparently insufficient milk-supply the fault was in the failure of the infant to suck properly. These cases usually would have been considered cases of insufficient secretion of the mothers; that this was not true was proved by the fact that all the mothers were able to pump off considerable amounts of milk after each feeding. The cases observed were for the most part in very young infants, and the cause he suggests is that previously brought forward by Finkelstein: the possibility of the late development of the sucking reflex in these infants. The most efficient treatment he found to be the substitution of shorter intervals of feeding, three hours instead of four hours. This was continued only two to three weeks, when a return could be made to the longer intervals.

Rosenstern¹⁰ and Langstein⁸ are both averse to any general change in breast-feeding to shorter intervals, although in especial cases, as here, it is indicated; in their opinion the long intervals of feeding have done much to make possible the present increase in prevalence of breast-feeding. Other therapeutic measures advised by Rosenstern in this condition are: a temporary "*allaitement mixte*" which may often be discontinued after ten to twenty days; the giving after each feeding of breast-milk which has been pumped off; the administration of small amounts of pepsin and hydrochloric acid.

Langstein⁸ advises buttermilk for "*allaitement mixte*" if the latter is necessary; and believes that it is unimportant whether the supplementary feeding be given after each nursing, or as separate feedings.

As a method for determining the amount of breast-milk taken by the infant the regular weighing before and after each feeding for two successive days is coming into general use; it is especially recommended by Langstein,⁸ Rosenstern,¹⁰ Jones¹¹ and others. Reuben⁶ considers this method less practical than the weighing of the infant before and after a week on exclusive breast-feeding and noting the gain or loss.

Engel¹⁵ has made an interesting observation relative to the souring of breast-milk. He finds that this depends to a large extent on the fat, and that the cream shows a much higher acidity than the whole milk.

On the subject of the wet-nurse problem, there have been interesting and practical studies by Hoobler, Talbot and Lee. Hoobler¹² reports the results of a successful experiment in the collection of human milk for hospitals, from women who came to the hospital once or twice daily. He believes that it is possible to obtain breast-milk in this way at a moderate price in any hospital, through cooperation with the Social Service Department.

Lee¹⁴ tells of the excellent results which were obtained in a series of foundlings under the care of wet-nurses. Of thirty-one infants, twenty-three developed well; of these many had been extremely atrophic infants.

Talbot¹³ describes the very successful wet-nurse directory established under the supervision of the Massachusetts Babies' Hospital.

ARTIFICIAL FEEDING

General

17. Howland: AM. JOUR. DIS. CHILD., 1913, v, 390.
18. Rosenstern: Ergebn. d. inn. Med. u. Kinderh., 1911, vii, 337.
19. Morse: New York Med. Jour., 1913, xcvi, 477.
20. Lederer: Ztschr. f. Kinderh., 1914, x, 90.
21. Schloss: Ueber Säulings ernährung, Berlin, 1912, Karger.
22. Leopold: Arch. Pediat., 1914, xxxi, 20.
23. Barhdt: Jahrb. f. Kinderh., 1913, lxxviii, 598.

24. Barhdt and Edelstein: *Ztschr. f. Kinderh.*, 1914, x, 303.
25. Langstein: *Jahreskurs f. Aerztl. Fortbild.*, 1913, iv, No. 6.
26. Rulison: *Arch. Pediat.*, 1913, xxx, 762.
27. Phillipson: *Monatschr. f. Kinderh.*, 1913, xii.
28. Reinach: *Ztschr. f. Kinderh., Ref.*, 1914, vii, 397.

Howland¹⁷ considers our guides in infant feeding in regard to the amounts to be given. He criticizes the caloric standard, as the energy quotient of 100 calories pro kg. body-weight was first determined on the basis of calorimetric observations made on children at rest. He has shown that the heat elimination of infants crying or making active movements is 18 to 39 per cent. greater than that of those at rest; so that by this method one cannot learn the total amount of energy that should be furnished the normal growing child. He criticizes also the statistical method, in which the intake of food of normal thriving breast-fed infants has been systematically measured for long periods. on the ground that the composition and hence the caloric value of breast-milk varies greatly.

Rosenstern¹⁸ has made clinical observations on many artificially fed infants, and has found that 100 calories pro kg. of body-weight is sufficient for a normal gain on diets which are poor in fat and rich in sugar; while on those with much fat and low sugar more calories are needed. He advises an increased energy quotient for premature and atrophic infants. Langstein^{*} comes to the same conclusion. The same authors discuss the importance of the various constituents of cow's milk, in the artificial feeding of the infant. The water content is of the first importance, the salts and carbohydrate next, gain in weight and water retention being to a large degree dependent on the salt and sugar content. Rosenstern believes that knowledge of this fact is of great practical importance at the present time, when so many of the therapeutic foods are based on the principle of a reduction of the whey content. The loss in weight of a child changed to a diet poor in salt is the greater the richer the previous diet was in this constituent. A child changed from a diet rich in salt to breast-milk, which is comparatively poor in salt, will show a loss in weight. Carbohydrates are absolutely essential to life. The minimum amount of sugar that it is safe to give varies with different children, but is placed by these authors at 1.5 per cent. Without carbohydrates a gain in weight is impossible. Protein is apparently necessary in smaller percentage than is sugar, as shown by its relatively low content in breast-milk. Fat they believe to be entirely replaceable by carbohydrates; children have been fed on fat-free mixtures for months without symptoms, in case the caloric needs are covered.

Czerny agrees that gain in weight depends on the carbohydrates, but does not agree that it is proven that fat may be entirely replaced

by carbohydrate without harm; Morse¹⁹ and others believe that fat is of great importance, especially to the young infant.

Lederer²⁰ has studied the importance of water to the infant metabolism.

The relation between artificial feeding and a decrease in the immunity to infections has been the subject of considerable study. Czerny² has studied the relation of natural immunity to different foodstuffs. He quotes the animal experiments of Weigert, which showed that those fed on high percentages of fat have the greatest resistance against tuberculosis, while those on high carbohydrates have the least. Czerny has found that children fed on diets rich in fats (including breast-milk) have the greatest resistance to infection, while children on diets rich in carbohydrates, but poor in fat, have the least natural resistance. The latter fact he attributes to the greater water content of the tissues on this diet; a high water content being always associated with low natural immunity. Kleinschmidt¹ studied this subject by observing in animals the effects of different foods on the formation of certain antibodies, such as hemolysins, agglutinins and bacteriocidins. He found that young dogs on diets rich in carbohydrates or fat did not necessarily show any diminution in antibody formation, but that the dogs who acquired disturbances of nutrition on these artificial diets did show a decrease in hemolysins, which returned to normal during convalescence.

Artificial Feeding of the Normal Infant

Morse¹⁹ advises feeding by the percentage method, as thereby greater individualization of cases may be practiced.

The simple dilutions of milk (one-third, one-half, two-thirds) with water or barley water, enriched with carbohydrate, are recommended by various writers: Rulison,²⁶ Philippon,²⁷ Reuben.⁶ They are in general use in Germany, and are becoming widely used in this country. On account of their simplicity they are generally used in feeding at Infant Welfare stations. The relative value of the various sugars is treated below in another connection. The early addition of fruit juices and vegetable purées to the diet (at the seventh or eighth month) has been recommended again by Langstein.²⁵ In the feeding of children from 1 to 3 years of age he urges the reduction of the amount of milk taken, the addition of larger amounts of fruit and vegetables, with meat in the second year, and the avoidance of eggs.

Efforts are being continually made to prepare a diet for normal children superior to the simple milk dilutions; the most important of this class are the Friedenthal milk and the "whey-adapted" milk of Schloss. Both were originated with the purpose of imitating breast-milk as nearly as possible. In both a marked dilution of the salt con-

tent is a principal feature. Friedenthal, according to Bahr^{23, 24} has ignored recent findings as to the dangers of fermentation of lactose, and those of a high fat content, and has simply attempted an imitation of the composition of breast-milk. Schloss, he says, at first used this milk, but not finding it successful, developed from it his own whey-adapted milk, which is in reality entirely different. Friedenthal's milk consists of the following ingredients:

Skimmed milk	330	c.c.
Water	660	c.c.
Lactose	68.9	gm.
"Molkerei" salts	1.89	gm.
Fat (in cream) to.....	4.5	per cent.

The "molkerei salts" consist of two parts KCl, one part K_2HPO_4 and one part KH_2PO_4 . These are added to bring the composition of the mixture in regard to the separate salts as near as possible to that of breast-milk. At first only the cream was pasteurized, the milk being sterilized by centrifuging; but as the bacterial count was found to be very high the milk also was pasteurized during July and August. Bad effects from the milk, even when showing an extremely high count, were not frequent. Bahr²³ believes that this has a bearing on the question of the relation of bacterial contamination of milk to summer diarrhea. In its composition as compared with that of breast-milk it shows equal percentages of fat and lactose, while those of proteid and salt are higher. This diet was given to 150 children; of these eighty-nine were considered in the review. Among these were healthy, newborn, premature and sick infants. The results as to gain in weight, confirmed by the good retention of nitrogen and ash in prolonged metabolism experiments, were very satisfactory. In the healthy children the average weekly gain was 123 gm. No immunity to parenteral infections is conferred by this food, but it is noticed that the infants pass through them with little disturbance of nutrition. Frequently there is vomiting, and the stools are often abnormal, apparently without clinical significance, resembling in this respect the stools of breast-fed infants. Bahr²³ and Edelstein conclude that Friedenthal's theory of the benefits of a food approximating breast-milk in composition has been proved true in practice, and that the food has been shown to be far superior to simple milk dilutions as a food for normal infants.

Langstein²⁵ warmly recommends the Friedenthal milk. Confirmation from other sources has not so far appeared; in a matter of this importance it is to be anxiously awaited.

The "whey-modified milk" of Schloss²¹ is essentially a diet rich in fat and proteid, poor in salt, with the addition of carbohydrates which

are not easily fermented. It resembles the group of substitutes for albumin milk to be later described; but differs in that it was developed in an attempt to imitate breast-milk. To milk diluted with twice the amount of water is added fat, in the form of cream, proteid in that of the preparations "nutrose" or "plasmon;" the carbohydrates added are a very finely ground maize flour and *Nährsucker* (dextrin-maltose). In addition a small amount of potassium chlorid is added. Schloss fed two hundred infants on this food for about a year with very good results; the development, color and stools all being normal.

Leopold²² describes the preparation of this food as recommended by Schloss and reports a series of thirty cases, which were, however, not normal; all had nutritional disturbances. In no case did he see harm from its use. It appeared especially indicated in young infants, while older children often showed no gain.

Reinach²⁸ has also used this food; his results in normal infants were but moderately successful when the food was used alone; when it was used as "*allaitement-mixte*" they were more successful. He, too, saw the weight stationary for long periods; it increased, however, when sugar was added. Of twenty-one cases of sick infants on this feeding, sixteen showed recovery.

ARTIFICIAL FEEDING OF THE SICK INFANT

29. Benfey: *Jahrb. f. Kinderh.*, 1913, lxxvii, 475.
30. Finkelstein and Meyer: *Monatschr. f. Kinderh.*, 1909, viii, 8.
31. Finkelstein and Meyer: *Jahrb. f. Kinderh.*, 1910, lxxi, 525.
32. Finkelstein and Meyer: *München. med. Wchnschr.*, 1911, lviii, 315.
33. Meyer: *Jahrb. f. Kinderh.*, 1913, lxxvii, 85.
34. Wilcox and Hill: *AM. JOUR. DIS. CHILD.*, 1913, v, 297.
35. Hoobler: *AM. JOUR. DIS. CHILD.*, 1913, v, 308.
36. Meyer: *Halbmonatschr. f. soziale Hygiene u. Prakt. Med.*, 1912, No. 9.
37. Nobécourt and Schreiber: *Bull. de la Soc. de Pédiat.*, 1913, xv, No. 7.
38. Ribadeau: *Nourrison*, 1913, i, 162.
39. Beck: *Klin.-therap. Wchnschr.*, 1913, xxv, 740.
40. Heim and John: *Ztschr. f. Kinderh.*, 1912, iv, 1; Heim and John: *Monatschr. f. Kinderh.*, 1913, xi.
41. Frank: *Monatschr. f. Kinderh.*, 1913, xii, 151.
42. Engel: *Deutsch. med. Wchnschr.*, 1913, xxxix, 1251.
43. Engel: *Jahrb. f. Kinderh.*, 1913, lxxviii, 299.
49. Hoobler: *Arch. Pediat.*, 1914, xxxi, 174.
50. Aschenheim: *Monatschr. f. Kinderh.*, 1913, xii, 229.
51. Steinitz and Weigert: *Monatschr. f. Kinderh.*, 1913, xii, 243.

The interest this year has centered about the group of albumin milk and its substitutes. Whey and whey-soup have also been used. There are few new publications on buttermilk or on malt-soup.

ALBUMIN MILK

Albumin milk has now been proved to be of the greatest value as a therapeutic food in the nutritional disturbances of infancy. This is shown not only by its widespread use, but also by the large numbers of substitutes and imitations, descriptions of which have dominated the literature on infant feeding for this year.

Benfey²⁹ gives a careful review of the literature on albumin milk from its introduction in 1909 until April, 1913. Finkelstein and Meyer, he says, in their first publication, described its essential qualities as consisting of a high percentage of proteid, with a moderately high fat content, and a very low percentage of the salts and of milk-sugar. The chief benefits of the food are a reduction of fermentation in the intestine, and a substitution for it of putrefactive changes, leading to the characteristic calcium soap stools. With the cessation of diarrhea a gain in weight is made possible; also an increase in tolerance to all foods occurs.

Finkelstein and Meyer^{30, 31} in their earliest publications, advised its administration at first without carbohydrate; this was to be added later only when the stools became normal. After much clinical observation they have, however, become convinced of the great dangers of too complete and too prolonged withdrawal of carbohydrates, as leading to marked initial losses in weight, with later stationary or gradually falling weight. In their later publications,^{32, 36} therefore, they advise that albumin milk without sugar should not be used; 1 per cent. of sugar should be given at first and this should be rapidly increased to 2 to 3 per cent., and later, if there is no gain in weight, to higher amounts. Benfey adds from his experience at Finkelstein's clinic that there albumin milk with less than 3 per cent. sugar is never used. As explaining this procedure, the authors maintain that in the medium of albumin milk, sugar is tolerated in amounts that cause trouble when given in other media; as sugar is essential for a gain in weight, this is one of the chief advantages of the food.

Benfey reviews, at some length, the results of different observers with albumin milk from the time of its introduction. As the first series of cases were all treated according to the first directions of the originators, that is, with a very late and meager addition of carbohydrates, Benfey believes that they do not give a fair picture of what can be accomplished with this food. The results were, on the whole, favorable, and many authors expressed the opinion that albumin milk is a valuable aid in all nutritional disturbances. The reports from other countries, as from France and America, have been less favorable than those from Germany; there, however, he believes, the fear of giving carbohydrates has persisted longer. In the series from these

sources, in which exact data as to dosage are given, Benfey has found errors in technic, especially in the giving of too little carbohydrate, or in beginning too late, or in withdrawing it a second time. In reports in which no data are given, he assumes that the same errors in technic are at fault. He quotes Finkelstein as saying that no one should express an adverse opinion on albumin milk, who has not followed the later instructions as to dosage. Benfey concludes that the general opinion of the majority of authors is that they can obtain results in certain cases with albumin milk which cannot be achieved with any other form of artificial nourishment. The chief criticisms of the food are:

1. Its costliness, if obtained at a laboratory, and its difficult preparation if it is made in the hospital or home.
2. Its disagreeable taste and appearance.
3. An alleged tendency to cause eczema, and also one to cause rachitis or Barlow's disease, if fed for too long periods.
4. Poor results obtained in disturbances resembling dysentery.

He adds a valuable résumé of the indications for use, and the technic of feeding of albumin milk according to the present status of experience.

Indications for Albumin Milk

Albumin milk he believes to be indicated in all disturbances of infants accompanied by diarrhea, including these disturbances when associated with parenteral infections; also in all nutritional disturbances not reacting to other forms of artificial feeding. This includes true bacterial enteritis, in which Finkelstein has achieved very good results in spite of some adverse criticisms by other writers. Only in "weight disturbance" (*Milchnährschaden* of Czerny) better results are obtained with mixtures rich in carbohydrates, such as malt-soup.

Technic for Use of Albumin Milk

1. In dyspepsia and decomposition: Weak tea only should be given for six hours; then albumin milk at the rate of 300 gm. in twenty-four hours with 3 per cent. *Nährzucker*. In mild cases and in older children even more should be given. The daily amount is then to be rapidly increased without respect to the stools or other symptoms until 180 to 200 gm. per kilogram of body-weight is given in twenty-four hours. After cessation of the diarrhea, the sugar is to be increased to 5 per cent.; when there is no further gain in weight, to 6, 7, or 8 per cent. In children over 3 months flour should be added in the amount of 1 per cent.

In subtoxic cases, or those on the borderline between dyspepsia and intoxication, the amount should be only 150 to 200 gm. for the first

twenty-four hours with 3 per cent. sugar; the increase should then be more gradual, as in intoxication.

2. Intoxication: Weak tea only is given for twelve to twenty-four hours; then for twenty-four hours ten feedings of 5 gm. of albumin milk with 3 per cent. sugar, after each of which large amounts of water or tea should be given. The amount should then be increased very gradually by 50 gm. daily, until severe diarrhea stops; after which a more rapid increase should daily be made until the amount of 180 to 200 gm. per kilogram body-weight is reached. At this point at latest, the carbohydrates should be increased; but if meanwhile the fall in weight has not stopped, carbohydrates should be added earlier. In case diminution of the toxic symptoms does not occur, the amount should be increased only to the point of 130 to 150 gm. per kilogram body-weight with 3 per cent. sugar; at this point one should stop until toxic symptoms disappear. An attempt to bring about lessening of the toxic symptoms by a second withdrawal of food is extremely dangerous and often fatal. Benfey warns against the use of albumin milk combined with any other food. It has been much used as "*allaitement mixte*" with human milk; but here he believes the results with buttermilk are better.

The cause of the beneficial results of albumin milk has been considerably discussed, especially in relation to the substitutes. The general result is a change in the predominating bacterial flora of the intestine; bacteria of the fermentative group lose the ascendancy, which is gained by those of the putrefactive group; this condition is far more favorable and permits the formation of soap stools with foul odor. The elements favoring this change are, according to the early publications, the high percentage of proteid, and the low percentage of salt and of milk-sugar.

Stoeltzner⁴⁴ believes that the success of certain substitutes proves that the diminution in salt and sugar, also the large amount of fat, are of minor importance; that the feature of albumin milk essential to its success is the high content of proteid and calcium.

Wilcox and Hill³⁴ report on results with a modification of albumin milk, in whose preparation skimmed milk was used, the fat content consequently being very low. In its administration they did not follow the rules laid down by Finkelstein, as they omitted the preliminary time of hunger or tea diet; did not add sugar at once, but only after an improvement in the stools. They used the albumin milk only as a corrective and only for short periods, as they found that gain in weight followed very slowly or not at all.

Hoobler³⁵ studied the metabolism of children fed on protein milk made in this way, having the following composition: proteid 2.8 per

cent., carbohydrates 2.4 per cent., fat .8 per cent. He found that on this large amount of proteid the nitrogen intake was increased over the normal, and its retention good, being 27 to 35 per cent. He quotes the important findings of Holt and Levene as to the clinical composition of the stools on diets high in protein, showing a decrease in acidity, together with one in the volatile fatty acids, a great increase in the soaps, with an improved retention of the mineral salts and a decrease in the amount of water lost.

G. Meyer³³ reports on the successful use of albumin milk in dispensary work; he favors a slight modification of technic, as follows: Children who are markedly atrophic should be given more than the usual 200 gm. per kilogram body-weight; sugar should not be added in larger amounts than 5 per cent.

Two more unfavorable reports on albumin milk have come recently from France. Nobécourt and Schreiber³⁷ think it illogical to suppress the lactose of the milk and add maltose. They believe the absence of sugar is dangerous. They administered the food in twenty-one cases, with good results in only two.

Ribadeau³⁸ saw bad effects, characterized by a sudden collapse with coma, after the use of albumin milk, even though he had followed exactly directions as to its use.

Beck³⁹ reports a series of 300 cases of nutritional disturbance treated with this food. He believes that there is at present no other artificial food which, in severe sickness, leads to recovery with such rapidity, certainty and frequency as does albumin milk.

SUBSTITUTES FOR ALBUMIN MILK

The faults of albumin milk previously referred to, particularly its expensive and difficult preparation, have limited its usefulness, especially in private practice. Here it is almost excluded except in cities with milk laboratories and among the rich. Its other disadvantages, such as its unattractive appearance and taste and its tendency to clump unless very carefully heated, are of less importance, but are definite drawbacks. Hence many pediatricians have been striving to originate foods without these disadvantages, yet incorporating its essential principles, and giving the same results. Many of these substitutes have been introduced, and for many of them results "at least as good" as those of albumin milk have been claimed; yet I believe until the results are more fully corroborated, those who can obtain albumin milk will continue to use it. To those who are not able to obtain it, one or the other of these simpler substitutes are recommended.

The first modification was that of Heim and John,⁴⁰ who on account of difficulty in obtaining good buttermilk used in its stead

skimmed milk diluted one-half or two-thirds with water, to one liter of which the curd, that is the proteid, fat and calcium, from two-thirds of a liter of whole milk was added after fine subdivision through a sieve. The essential feature is then the substitution of skimmed milk for buttermilk. They give the histories of cases receiving this feeding, with results resembling those of albumin milk.

Frank⁴¹ made comparative metabolism experiments comparing children fed on diluted whole milk with three children fed on milk enriched with casein and fat as above. The conclusions are that on this feeding carbohydrate absorption is good, the retention of nitrogen normal, the fat resorption normal.

Engel^{42, 43} finds that Heim and John's preparation is still too difficult for practical use, as it involves the fine subdivision of the curd through a sieve. This he attempts to avoid by very careful dosage of the lab ferment; by this means he obtains a curd with fine flocculi. He then dilutes the mixture with an equal amount of water, and after the casein flocculi have settled, pours off one-half of the supernatant fluid. He obtains a mixture in which the whey is diluted one-half, while there is a relatively high percentage of proteid, fat and calcium. He advises the use of this casein milk in the same amounts as those advised for albumin milk, with the same additions of sugar.

On comparison of the composition of this diet with that of albumin milk, it is shown that the percentages of proteid and fat are the same, but that those of sugar and calcium are higher in the casein milk. His results, in nine months' use, are, he says, as good as those with albumin milk.

Hoobler⁴⁹ has used a modification in which he employs casein flour. This he adds in the amount of 10 gm. to one pint of fat-free buttermilk and one quart of warm water. In some cases he uses the artificial buttermilk, which contains fat. With this preparation he has attained very good results. Its chief advantages are its cheapness, and ease of preparation, recommending it for private and dispensary practice.

Aschenheim,⁵⁰ led by the importance of calcium in the formation of the firm soap stools, tried adding calcium in the amount of 7 to 10 gm. in 10 per cent. solution to the diet. He gave it in all types of nutritional disturbances, and never saw any unfavorable symptoms; the results were fairly good, but not to be compared with those of albumin milk. The best results were obtained in dyspepsia, the worst in dyspepsia caused by parenteral infections.

Steinitz and Weigert,⁵¹ seeking a diet very poor in fat for use in acute disturbances have used "whey-soup," which is merely whey to which 4 per cent. mondamine is added. They use it with good results in the same way that Stolte used buttermilk with mondamine, giving only one to three feedings daily of this preparation, the other feedings being simple milk dilutions.

STARVATION

Some extremely interesting work is that done chiefly by Finkelstein, Meyer, Rosenstern and Langstein on the subject of the importance of starvation to the infant. A good deal of this work dates back to 1911 and 1912, but has not been reviewed in this journal.

In an excellent review of all the work done on this subject, together with an account of his own clinical observations, Rosenstern¹⁸ says that at the present time the good effects of starvation are so generally accepted that its dangers are neglected. The latter are not important to the healthy infant, but are extremely great to the sick child. In atrophic babies, hunger often leads to a fatal collapse; so that in these cases a tea or water diet should not be given at all, but small amounts of food from the beginning. Also in overfed children, especially those previously on a high percentage of carbohydrates, starvation will sometimes lead to an extreme and even dangerous loss in weight. Starvation as a therapeutic measure is most successful in acute disturbances, such as dyspepsia and intoxication; it is dangerous in chronic and recurrent affections. When used as a therapeutic measure, the following procedure should be employed: complete hunger for a short space of time, followed by small amounts of food, which are rapidly increased. The opposite procedure, with a gradual diminution in the amount of food given, leads, as he demonstrates by charts, to much greater losses in weight. He warns against this method, as well as against the starving of an infant many times in succession. Langstein⁸ has confirmed and amplified this work.

The qualitative starvation in different foodstuffs is considered by both; water, sugar and salt starvation are the most important and dangerous.

THE NUTRITIONAL DISTURBANCES OF INFANTS

52. Dunn: *Boston Med. and Surg. Jour.*, 1913, clxviii, 161, 168.

53. Finkelstein: *Ztschr. f. Kinderh.*, 1913, vii, 67.

54. Smith: *Boston Med. and Surg. Jour.*, 1913, clxix, 756.

55. Koplik: *Arch. Pediat.*, 1913, xxx, 484.

The majority of American authors believe that our present classifications of the nutritional disturbances are temporary and will soon be changed.^{55, 19} Dunn⁵² classifies them, on an etiological basis, into two chief types:

1. Those caused by foodstuffs: fat, carbohydrates, proteid, salt. Within this main group he includes two sub-groups:

a Those caused by abnormal digestion or absorption of several foodstuffs, especially fat and proteid, shown by vomiting and dyspeptic stools, the treatment for which consists in a reduction of these substances.

b A little understood group, characterized by intolerance to salt, fat and milk-sugar; which is best treated with a diet containing little fat and sugar, and much casein.

2. Disturbances caused by bacterial infections. Of these the majority of the causative agents, except dysentery and gas bacilli, are unknown. They are best treated with buttermilk.

Smith⁵⁴ gives a similar classification. Finkelstein⁵⁵ has expanded and modified his former classification, without, however, changing its main features. He considers the introduction of the term "nutritional disturbances" as of value; but thinks that at present too many heterogeneous conditions are included under the term. He divides the "alimentary disorders" into two main classes:

1. Nutritional disturbances due to an error in diet; that is, to an exogenous cause.

2. Nutritional disturbances from endogenous causes, such as essential anomalies of growth and development, and to constitutional diseases, such as rachitis and spasmophilia.

Finkelstein does not believe that these disturbances can best be classified on an etiological basis, as has been done by Czerny; for he shows that in the causation of any disturbance many factors combine as nutrition, infection, constitution, heat, etc., and that rarely has a disturbance but one cause. Hence he uses as a basis for his classification the essential clinical features, using the etiology, however, as a secondary means of differentiation. The group of nutritional disturbances of exogenous cause he divides into (1) dystrophies, or conditions due to faults in diet, without marked disturbances of the gastro-intestinal function. This includes several types of the "*Bilanzstörung*" of his older classification. (2) Alimentary toxicoses, which do show gastro-intestinal and metabolic disturbances, such as diarrhea and marked losses in weight. These include the less and more serious conditions: dyspepsia, decomposition and intoxication. All these may arise from a purely alimentary basis; or from a mixed cause, alimentary and infectious. In disturbances from the latter cause the prognosis is far more serious, as the ability of the organism to secrete digestive juices and ferments is decreased and internal metabolism is attacked. He believes that the colloids in close relation to carbohydrate and salt metabolism are so changed that the salt and water content of the organism is threatened.

Etiology

56. Howland: AM. JOUR. DIS. CHILD., 1913, v, 390.

57. Langstein: Jahreskurs. f. Aertzl. Fortbldg., 1913, vii, No. 6.

58. Feer: Jahrb. f. Kinderh., 1913, lxxvii, 1.

59. Jörgensen: Monatschr. f. Kinderh., 1913, xii, 386.

60. Wood: Arch. Pediat., 1914, xxxi, 259.

61. Bendix: *Ztschr. f. Kinderh.*, 1913, vi, 468.
62. Klotz: *Ergebn. d. inn. Med. v. Kinderh.*, 1912, viii, 593.
63. Morse: *Jour. Am. Med. Assn.*, 1913, x, 875.
64. Talbot: *Arch. Pediat.*, 1913, xxx, 244.
65. Southworth: *Arch. Pediat.*, 1913, xxx, 732.
66. Holt and Levene: *Med. Klin.*, 1913, ix, 258.
67. Neuhaus and Schaub: *Ztschr. f. Kinderh.*, 1913, vii, 310.
68. Lust: *Jahrb. f. Kinderh.*, 1913, lxxvii, 383.
69. Calvary: *Ergebn. d. inn. Med. u. Kinderh.*, 1913, x, 699.
70. Hahn: *Jahrb. f. Kinderh.*, 1913, lxxvii, 405.
71. Hess: *AM. JOUR. DIS. CHILD.*, 1913, v, 457.
72. Grulee: *Jour. Am. Med. Assn.*, 1913, lxi, 1022.
73. Gildemeister and Baerthlein: *Deutsch. med. Wchnschr.*, 1913, xxxix, 982.
74. Vaughan: *Jour. Am. Med. Assn.*, 1913, lxi, 1761.
75. Baerthlein and Huwald: *Deutsch. med. Wchnschr.*, 1914, xl, 478.
76. Bauer, Ellenbeck and Fromme: *Arch. f. Kinderh.*, 1913, lxi, 35.
77. Siegel: *Arch. f. Kinderh.*, 1913, lx-lxi, 689.
78. Weihe and Shürer: *Ztschr. f. Kinderh.*, 1914, x, 36.
79. Smith: *Boston Med. and Surg. Jour.*, 1913, clxix, 756.
80. Kendall: *Boston Med. and Surg. Jour.*, 1913, clxix, 741, 749, 754.
81. Vincent: *Arch. Pediat.*, 1914, xxxi, 53.
82. Vincent: *AM. JOUR. DIS. CHILD.*, 1914, vii, 97.
83. Vincent: *Am. Jour. Obst.*, 1913, lxviii, 1204.
84. Keuper: *München. med. Wchnschr.*, 1914, lxi, 474.
85. Bowditch: *Arch. Pediat.*, 1913, xxx, 866.

The views of the different schools of pediatrics as to the etiology of the nutritional disturbances of infants are becoming gradually reconciled, as there has come to be a general agreement that the principal cause may be either one of two general causes: food or bacterial infection. In Germany the chief prominence is given to the influence of the different food elements, together with the predisposing action of certain other factors, such as hot weather and parenteral infections; yet there, too, there has been a great increase in interest in the intestinal infections, especially of the dysentery group. In America, on the other hand, while the influence of the different bacterial infections is still considered of the greatest importance, especially in the etiology of the summer diarrheas, yet there is greater interest than before in the harmful action of the foodstuffs.

Influence of Food and Foodstuffs

Howland⁵⁶ gives a valuable critical review of our present knowledge of the rôle of the different elements—proteid, fat, carbohydrate and salt—in the causation of these disturbances, and shows how on each in turn has fallen the blame. The damaging influence of sugar and salt, now given the principal place as causing the acute disturbances, may, he considers, be exaggerated.

Langstein⁵⁷ and Feer⁵⁸ both believe that separate food elements should no longer be considered the primary causes of the nutritional disturbances, but rather a faulty correlation between them. Lang-

stein believes the ingredient of chief importance in cow's milk is the whey (or salts and sugar in solution). He quotes Meyer's well known "whey exchange" experiment in proof of this. The combination of a high whey content with a high sugar and low proteid percentage causes the greatest number of nutritional disturbances. Increase of the proteid reduces the danger. A high percentage of whey can be tolerated if the sugar is low; of such diets buttermilk is an example. The cause of this is unknown, according to Langstein; two possibilities may be considered: that the whey is injurious to the intestinal wall, and causes a greater permeability for various substances; or that the whey stimulates carbohydrate fermentation.

Feer, on the other hand, thinks the relation between fat and whey is most important; mixtures rich in both fat and whey are harmful, but after removal of the fat they are well borne.

Salts

The rôle of the salts, in combination, as above, with sugar or fat, is at present in Germany placed in the highest position of importance as the damaging substance in cow's milk. Its reduction is the foundation both of the proposed normal foods for infants, such as the Friedenthal milk and Schloss's whey adapted milk, and of the chief therapeutic foods, such as albumin milk and its substitutes. The chief theory of its harmful action is the second named by Langstein: that it favors acid fermentation by bacteria of carbohydrate if this is present in large amount, with the production of an excess of the low fatty acids and the consequent irritation of the intestine. Large amounts of proteid change the process to one of putrefaction.

Salt fever, or the temperature previously caused by parenteral injections of salt solution, has again been proved by Jörgensen⁵⁹ not to occur, if the water used as diluent for the salt solution be freshly distilled and sterile. This had previously been shown by several observers, among them Samelson and Bendix. Hence a direct fever produced by salt seems excluded. Wood⁶⁰ has reviewed the rôles of the salts in the infant's nutrition.

Carbohydrates

The action of the carbohydrates as related to that of the salts has already been reviewed. Some difference of opinion still exists as to the comparative harmfulness of the different sugars. Lactose is recommended by Morse¹⁹ as the least harmful. The various combinations of maltose with dextrin are most often advised by German authors. Calvary considers lactose as good as cane-sugar. Bendix⁶¹ fed different forms of sugar to thirteen infants in order to determine which caused the least trouble. He found, contrary to the usual findings,

that cane-sugar caused the least fermentation, lactose the most, while maltose held a position midway between the two. Maltose, however, led to a greater gain in weight. He strongly advises the use of cane-sugar on account of its cheapness. Klotz⁶² has found that the various flours vary greatly in their properties but so far the indications for the various flours are not certain.

As to the much discussed "sugar fever," Kleinschmidt⁶³ showed that on intravenous injection in rabbits of an isotonic dextrose solution, the diluent of which was freshly distilled water, he obtained no rise of temperature. With an isotonic lactose solution he did, however, obtain a rise of temperature which he believes may be due to bacteria in the milk-sugar.

Fat

The rôle of fats as an exciting cause of the nutritional disturbances is given varying importance by different writers. The point is still unsettled whether acute dyspepsia is or is not caused by fat. Feer, as before shown, believes that fat in a medium containing a high whey percentage may cause acute disturbance. Dunn⁵² believes that there are acute disturbances due to fat, shown by vomiting and dyspeptic stools. Talbot⁶⁴ writes that there is an indigestion due to fat, the symptoms of which may be identical with those of one caused by sugar or protein, so that information as to the cause must be drawn from the vomitus and the stools. The vomitus he describes in these cases as creamy, while the stools macroscopically show soft curds, and microscopically much fat and soap. He adds the description of a staining method by means of which the proportionate amounts of fat, fatty acids and soaps can be determined. The action of fat as tending to induce vomiting and delay of food in the stomach has long been considered well established. The comparison of the gastric mobility with different foods by Ladd¹²⁷ tends rather to show that fat has less effect in the latter direction than casein.

The chief disturbance caused by fat is still considered that chronic condition known as "*Milchnährschaden*," "*Bilanzstörung*," or "weight disturbance." This is reiterated by Finkelstein, Howland, Langstein, Feer and others.

Southworth⁶⁵ calls attention to a closely related symptom, the ammoniacal odor of the diaper in certain infants receiving a large amount of fat. The explanation, he believes, is to be found in the metabolic changes described by Czerny in that condition. The essential change is an increase in acid formation, and the using up to neutralize it of fixed alkalies and of ammonia. The ammonia salts are excreted in the urine, to which they give the characteristic odor. As

the acid may also be neutralized by alkali taken by mouth, he finds that the trouble readily yields on the administration of alkalies while the percentage of fat is reduced. He reports five cases, fed on high percentages of fat, showing an ammoniacal odor of the urine which disappeared on this treatment.

Proteid

Morse¹⁹ does not believe that proteid is entirely harmless, while most of the German writers, among them Langstein, do consider it so. Combé has described a dyspepsia caused by albumin. Holt and Levene⁶⁶ have found that large amounts of casein by mouth can cause a rise in temperature. During the course of experiments in which a "synthetic food" very rich in casein was fed, they observed five times a rise in temperature, which continued until the food was changed, but then subsided to normal. This fever only occurred when 6 per cent. casein had been administered, with very small amounts of milk. Preceding the rise by three or four days and accompanying it, there was in all cases a retention of the chlorids. Other causes for this fever, such as salts, or a possible change in the intestinal flora, the authors believe are excluded. They call attention to the parallelism between this fever and that produced by Vaughan by the parenteral injection of proteins.

The association of anaphylaxis with some of the disturbances caused by cow's milk has always been a field for speculation; but so far the evidence has been very meager and inconclusive. Neuhaus and Schaub⁶⁷ report an interesting case, suggestive in this connection. A healthy child who had previously been breast-fed, but who had probably received small amounts of cow's milk, became very ill when he received a large amount of cow's milk. The symptoms were suggestive of anaphylactic shock, and there were large numbers of eosinophils in the stools. After recovery, a similar attack was induced by feeding casein from cow's milk, while casein from breast-milk and the whey from cow's milk had no effect. Later the child showed perfect tolerance to cow's-milk casein.

Hypersensitiveness to cow's milk could not exist without a passage of protein unchanged through the intestinal wall; this has been proved not to occur in the normal infant after the first weeks. That an increased permeability of the gastro-intestinal epithelium for foreign proteid occurs in children with nutritional disturbances has been proved by Hahn and Lust. Lust⁶⁸ fed different forms of foreign proteid to children with such disturbances, and then employed the following tests to determine whether or not the protein had passed through the intestinal wall unchanged: the urine, and in some cases the blood serum, were tested with a serum having a strong precipitation titer for

the protein which had been fed; also guinea-pigs were injected with the urine and after three weeks tested with the homologous protein for sensitization. He also studied the permeability in animals in which a gastro-enteritis had been produced by a strong sugar solution. In the experiments on infants he found that egg albumin passed through the wall nine times out of sixteen cases of acute and chronic nutritional disturbances, while ox serum passed once only out of seventeen cases, the passage being most frequent in acute intestinal disturbances, especially intoxication. The normal protective forces of the organism against the absorption of unchanged protein consist in two things: digestion of the proteid by gastric and pancreatic juices; and the normal resistance of the epithelial cells of the intestine to the passage of the protein. In nutritional disturbances, as the digestive juices are present, the fault must lie in the decreased resistance of these cells. He claims for his method considerable clinical value as a functional test of the condition of the intestine in nutritional disturbances. Hahn⁷⁰ has brought additional evidence to the same point, in his study of the passage of antitoxin bound to heterologous protein. It had been previously shown that the normal infant will absorb antitoxin given orally if bound to a homologous proteid, that is, if present in its mother's milk; but will not absorb it if bound to a heterologous protein, that is, horse serum. Hahn used Römer's test for the presence of antitoxin in the blood of infants to whom he fed horse serum antitoxin. Out of twenty-three cases all showing acute nutritional disturbances, there was in five a passage of antitoxin into the blood.

Vaughan⁷⁴ suggests an interesting possibility as to the cause of infantile diarrhea. He calls attention to the fact that peptone and other decomposition products of proteid cause symptoms of disease, and that "sensitization may result from the absorption of undigested or partially digested proteins from the alimentary tract. Whether or not the summer diarrheas of infancy ever originate in this way is a question to which a positive answer cannot be given. There are some good reasons for suspecting that the lowered vitality of the infant by excessive heat may lead to the absorption of undigested proteins, and in this way cholera infantum and kindred diseases may be induced."

It seems to me not quite clear from these guarded statements, whether the possibility suggested is that of an anaphylaxis to milk, due to the passage of its unchanged proteins into the blood, and the consequent development of hypersensitiveness; or that of an absorption of toxic split products of protein through the intestinal wall. The latter is the possibility spoken of by Grulee⁷² in the discussion to the above paper, and in a further article on the etiology

of ileocolitis. He recalls the fact that it has now been proved that salt and sugar on parenteral injection do not cause fever, thus undermining Finkelstein's theory that it is the abnormal absorption of these substances unchanged that produces the metabolic changes present in the nutritional disturbances. Salt and sugar in large amounts by mouth do, however, cause fever; Grulee suggests the possibility that these substances if given by mouth cause a change in the intestinal mucosa which allows absorption of the toxic products of protein decomposition from the intestine always present there. These may be endotoxins from bacteria, or may be the product of bacterial decomposition of protein. He suggests the intestinal mucus as a source of protein poisons independent of the food. Zahorsky,⁷⁴ in the discussion of Vaughan's paper states his belief that one form of diarrhea at present believed to depend on fermentation of the sugars, may possibly be due to absorption of the toxins mentioned by Vaughan. These theories, connecting the nutritional diseases with the protein toxins and with anaphylaxis are fascinating, but lack clinical and experimental proof; so that at present they remain only in the realm of conjecture.

The casein curds occasionally present in the stools of infants on unboiled milk continue to be the object of study. Hess⁷¹ has studied the site and causes of their formation. He concludes that there are several methods of inhibiting their formation: boiling of the milk (pasteurization does not prevent), the addition of sodium citrate, sodium bicarbonate or calcium citrate. The site of formation is apparently the stomach for he has found that the inside of these curds is never bile-stained; and in addition that a child who regularly passed curds when on unboiled milk no longer passed them when the same food was fed into the duodenum through a duodenal catheter. He found that some children, out of many on the same food, passed them much more frequently than others. He believes them to have little clinical importance, as their presence has no influence on the general development.

Influence of Bacteria

The bacteriological examination of the stools of infants with nutritional disturbances has long been an extremely confused field of research. Many different organisms have been described as occurring in connection with the same clinical symptoms; besides this, there has been lack of correspondence between clinical symptoms and bacteriological findings. From this confusion there has gradually emerged one fairly well defined clinical picture, called by different names: enteritis follicularis, ileo-colitis, dysentery-like diarrhea, etc., and characterized by fever, prostration, diarrhea with blood, mucus and pus in the stools, and a tendency to spread by contagion. In Germany much has been

written this year on this type of diarrhea, and the tendency is to confirm the earlier findings of American authors as to the frequent occurrence of dysentery and pseudo-dysentery organisms in these cases. In America, on the other hand, this clinical syndrome is associated with bacterial infection in general; and other organisms, especially the gas bacillus and the streptococcus, besides the dysentery and pseudo-dysentery bacilli, have been found closely associated with it. One point, not yet settled to my knowledge, is the relative importance and frequency of this type of disturbance in proportion to the entire number of cases of diarrhea which occur.

This form of diarrhea has long been recognized in Germany as an entity, but the tendency has been to consider it as only rarely a specific infection, and more usually merely the result of prolonged injury by food, leading to anatomical changes in the intestine. This theory still prevails in the minds of most of the writers on the subject, as shown by their failure to make direct mention of specific infection as a cause of the disease.

Gildemeister and Baerthlein⁷³ made a systematic examination of the stools of 120 normal infants, and of seventy infants showing diarrheal disturbances. They did not study the cocci nor anaerobic organisms. For the differentiation of dysentery bacilli they used the usual cultural tests. The feces for examination they obtained by inserting a small sterile glass tube with rounded edges into the rectum. Among the seventy sick infants they found dysentery bacilli of the Y-type nine times; paratyphus four times; bacillus enteritidis Gärtner, once. In all the cases in which dysentery bacilli were found the stools were very loose and contained mucus and blood. They did not, however, find the bacilli in all the cases showing these symptoms. Of the 120 normal cases, only two showed dysentery bacilli; the brother of one of these had clinical dysentery. The authors believe that some external factor, such as a change in diet may be necessary to give the organism pathogenic qualities.

They also found proteus, pyocyaneus and coli mutabile bacilli, besides a strain not previously described, more frequently in sick than in normal infants, but decline to draw conclusions.

Baerthlein and Huwald⁷⁵ continued the same study last year, using the same technic. Among seventy-two children they found dysentery bacilli twenty-one times, paratyphus seven times, pyocyaneus twelve times. They also found dysentery bacilli in one normal case. Agglutination of the homologous strain was positive in eleven cases. Few of the strains were of the Flexner group, which they consider rare in Germany. Clinically these twenty-one cases showed fever, prostration, great loss in weight and numerous defecations with blood and mucus.

Siegel⁷⁷ analyzes the clinical symptoms in the eight cases previously reported by Gildemeister and Baerthlein. In all but one there was blood and mucus in the stools. At post mortem the findings were those of enteritis follicularis; in only one was there loss of tissue. He concludes that there is a close relation between Y-dysentery infection and follicular enteritis.

Bauer, Ellenbeck and Fromme⁷⁶ report an epidemic in an asylum, in which the agglutination reactions in especial were studied. Artificially fed children only were attacked; of 29 children on the bottle, 22 showed a positive agglutination reaction for the Y-dysentery organism; of these 11 only had clinical symptoms. In 9 of these 11, dysentery bacilli were found in the stools. The epidemic broke out with great suddenness, all the children but one in one of the wards being affected. The authors conclude that the agglutination reaction is specific; namely, that a positive reaction is only obtained in cases which have or which have had dysentery; a negative reaction under one year does not, however, exclude dysentery. Infants, they find, are very susceptible, and strict isolation should be used.

Weihe and Schürer⁷⁸ give an interesting review of the question of dysentery infection in infants in Germany. They find that the leading text-books make very little mention of it. Two epidemics have been reported by Jehle and Leiner, but for the most part the reports of American investigators have not been corroborated. This they explain in part by the fact that the American authors in their reports did not distinguish between true primary bacterial infection and nutritional disturbances as well as parenteral infections. They also believe that the great labor involved in the study of these cases has deterred many from it. The authors examined the stools of eighty-five children with intestinal disease, twenty-two of whom showed clinical symptoms suggestive of dysentery. In eighteen of these they found pseudo-dysentery bacilli, for the most part of the Y-group. They consider that blood in the stools should always be considered a suspicious symptom, and that all cases showing it should be isolated. Agglutination tests in their cases were negative or at very low dilutions. They believe that all forms of the nutritional disturbances, such as decomposition, intoxication, etc., can be caused by it. At necropsy the cases showed the typical findings of enteritis follicularis.

Keuper⁸⁴ reports an epidemic of twenty cases, also two sporadic cases. In the majority of these the organism of Kruse was found. He insists especially on a long isolation period; that negative bacteriological findings on two successive days are not sufficient to warrant discharge; and that this organism, like the typhoid bacillus, may persist for long periods in the intestinal canal after clinical recovery. He

concludes that, as infants do not form agglutinins with any regularity, the serum test is useless for diagnostic purposes.

American authors have found not only organisms of the dysentery and pseudo-dysentery groups in infectious diarrhea, but also the gas bacillus, and probably the streptococcus; and believe that still others, as yet unknown, are also at times to blame.

Smith⁷⁹ says that the symptoms in all the infectious diarrheas are the same; they are those already described above in the German publications on enteritis follicularis. These infections can only be classified by means of a bacteriological examination of the stools, which is especially necessary as the treatment depends on the causative agent. In the dysentery infections high carbohydrate percentages should be fed with low protein; while in gas bacillus infection the sugar should be greatly increased and high protein percentages should be given. He says that a number of cases not showing the gas bacillus in the stools, did well on this treatment.

Bowditch⁸⁵ reviews the work of the Boston Floating Hospital in the study of the bacteriology of the intestinal diseases of infants for the past three years. He shows that different bacteria have predominated in different years.

Kendall⁸⁰ reports more in detail the same study, and speaks also of this variation from year to year. He believes that less is known of the etiology of summer diarrhea than ever; that previously a disturbance showing blood and pus in the stools was thought always to be caused by the dysentery group, but that it is now known that similar symptoms may be caused by a variety of intestinal bacteria; also that in cases with these symptoms, pathogenic bacteria may be absent.

In 1910 dysentery infections predominated, constituting 75 per cent. of those in which an organism was isolated. The gas bacillus and streptococcus were less frequently found.

In 1911, on the other hand, the streptococcus was present in 78 out of 146 cases; dysentery bacilli in 18, the gas bacillus in 33.

In 1912 the gas bacillus predominated, 53 out of 135 cases showing this, while dysentery was only present in 5 and the streptococcus in 6. The conditions necessary for the development of gas bacilli are: an excess of carbohydrate, and a deficiency of organisms capable of forming lactic acid in sufficient volume to inhibit their growth. The treatment in these infections which is theoretically correct, and which has proved itself of value is:

1. Restriction of carbohydrates.
2. The introduction of lactic acid in buttermilk, or of lactic acid producing organisms.
3. An increase in protein.

He shows that the pathogenic bacteria especially of the dysentery group may be found in normal cases.

Vincent^{81, 82, 83} studied the action of bacteria in the etiology of diarrhea from a new point of view: that of the bacteria growing in raw and in boiled milk. This work has not, so far, been confirmed.

So much for the rôle of bacteria as the direct causes of intestinal disease in infants.

Their secondary rôle, through action on foodstuffs, has long been believed by the German school to be extremely important, especially as regards the fermentation of carbohydrate by certain bacteria, apparently favored by the presence of a high percentage of salts. This view is held without change, and is expressed in most of the publications cited on albumin milk and its substitutes.

Influence of Parenteral Infections on Nutritional Disturbances

86. Meyer, F.: Hospitalismus, Berlin, 1913, S. Karger.

87. Meyer, F.: Ztschr. f. Kinderh., 1913, vii, 233.

88. Meyer, F.: Berl. klin. Wchnschr., 1913, I, 775.

89. Müller: Abstr. in Jahrb. f. Kinderh., 1913, lxxiv, 450.

90. Langstein: Ztschr. f. Kinderh., 1913, vii, 193.

91. Chapell and Brown: AM. JOUR. DIS. CHILD., 1914, vii, 380.

92. Triboulet: Bull. Soc. de Pédiat., 1913, xv, 281.

This year great interest has been shown in the marked influence exercised by infections, especially of the respiratory and urinary tract, on the origin and course of the nutritional disturbances in infants.

Meyer^{86, 87, 88} has written a great deal on the subject. "Grippe" is a clinical term which he uses to include infections of the respiratory tract of non-specific etiology, including pharyngitis, coryza, otitis and bronchitis. It is, he thinks, the infection most disturbing to the normal nutritional condition, causing loss of appetite and all types of disturbances: dyspepsia, intoxication and decomposition. Next in importance is pyelocystitis. The younger the infant, the more easily does the disturbance arise; also the diet has an influence, as such disturbances are more frequent on those diets tending in themselves to cause fermentation and diarrhea, such as those with a high sugar and salt percentage. Meyer⁸⁸ found that in dogs in whom severe nasopharyngeal infections were produced, the secretion of gastric juice was greatly reduced. He believes that other secretory activities are also diminished during infections, and that this may explain the close relation between them and disturbances of nutrition.

The importance of respiratory infections or "grippe" in infants' hospitals or asylums as preventing success in feeding cases has long been studied. Heubner pointed out their importance fifteen years ago, and showed that they were an important factor in the general condition called hospitalism. During the present year much work has been

done on the prevention of these infections. Meyer^{86, 87} finds that in infant hospitals and asylums the mortality is greater from respiratory infections than from nutritional disturbances. He finds that no child remaining in a certain infant asylum over one month fails to develop some form of infection, while those remaining longer show, on an average, one such a month. As many children are necessarily admitted with respiratory infections the question of greatest importance is, how to prevent transmission of the infection from one child to another. This involves the question of the usual way in which such infections are carried, whether by contact or by air infection. Though the theory of contact infection is at present most generally accepted, Meyer believes that many things speak for an air transmission, especially of respiratory infections. He used Lesage's fundamental idea that infections are usually air-borne and that currents of air are instrumental in spreading them (Müller⁸⁹), in the construction of an isolation ward. This showed a central aisle with a row on either side of compartments or boxes separated by partitions of glass, or gauze stretched on frames, 6 feet high. The ventilation in the ward was reduced to the minimum consistent with having the air fit for use. Beyond the usual washing of the hands after handling each infant, no measures against contact infection were used; no change of gowns was made except in the case of whooping-cough, measles and varicella cases. Further precautions were the avoidance of much movement and talking in the rooms, and the prevention of infection from physician or nurse if suffering with coryza or bronchitis, by means of their withdrawal from duty or by their wearing a gauze mask. The results were extremely successful; in two wards thus fitted up, 106 infants were treated during the course of a number of months; of these fifty-two were suffering with respiratory infections on entrance. In the two wards there were but two new infections, showing a tremendous reduction in comparison with the number of new infections in the other wards. Twenty cases of whooping-cough and five cases of measles were also treated with no secondary infections; varicella was, however, conveyed five times, confirming the experience of Lesage. The box system also showed itself incapable of preventing the spread of diphtheria bacilli from carriers; these were transmitted fifteen times. Cases of clinical diphtheria were few. The nutritional results were extremely good; of healthy children over 1 month, all gained well. Many children under 1 month on simple milk mixtures thrived, which Meyer believes is rare in infants' hospitals and asylums. Very good results were seen in children who in the other wards had suffered from recurrent infections with consequent disturbances in nutrition; in the boxes, where such infections were avoided, the weight showed an immediate and steady rise.

This article is extremely interesting as suggesting means for the prevention of these hospital infections. It is doubtful, however, whether the method could be used unmodified in the American summer climate.

Chapell and Brown⁹¹ also emphasize the importance of respiratory infections in hospitals; they believe that the spread of contagion both by contact and by air infection should be guarded against. As a prophylaxis against infections of the respiratory passages they have tried a systematic biweekly douching of the posterior nasopharynx with a special syringe. This is so constructed that danger of forcing fluid into the eustachian tubes is avoided. They report a marked reduction in the number of infections in the wards where this douche was used, as compared with the control wards.

Triboulet⁹² is so convinced of the danger to infants of the infections to which they are exposed in hospitals, that he advises the exclusion from infants' hospitals of both normal and atrophic infants. Only infants with acute disturbances should be admitted, their stay should be as short as possible, and they should be isolated in "boxes" to prevent the spread of contagion.

Langstein⁹⁰ also believes that in the course of acute infection, the digestive juices are decreased, and that there is some change in the cells so that the ability to bind water is injured. As a diet in acute infections he warns especially against one rich in carbohydrate and salt and advises one with a high percentage of proteid. Albumin milk is here indicated; if this is not obtainable, he advises a milk mixture with little sugar, and with the addition of some preparation of proteid such as nutrose or plasmon. He criticizes the administration of malt soup in pyelitis; this has been recommended on account of its high alkalinity. He believes that on account of its high percentage of sugar it is very dangerous in acute infections. Two symptoms which are especially difficult to combat in infectious diseases are vomiting and anorexia. Both of these he treats by feeding with a stomach-tube, with good results. Rosenstern¹⁰ treats the anorexia of children with acute infections by the giving of concentrated albumin milk. This can safely be given after the third month; by this means he has succeeded in feeding children with pneumonia, cystitis and pertussis so that there was no loss but even a gain in weight during the infection.

The Influence of Heat on Nutritional Disturbances

93. Rietschel: *Jahrb. f. Kinderh.*, 1913, lxxviii, 312.

94. Schereschewsky: *Arch. Pediat.*, 1913, xxx, 916.

95. Wolff: *Jahrb. f. Kinderh.*, 1913, lxxvii, 569.

96. Zahorsky: *AM. JOUR. DIS. CHILD.*, 1913, vi, 289.

97. Bleyer: *AM. JOUR. DIS. CHILD.*, 1913, vi, 319.

98. Knox: *Arch. Pediat.*, 1913, xxx, 191.

The complicated problem of the relation of hot weather to nutritional disturbances is still a field for controversy.

Rietschel,⁹³ who has written so much on this subject, has given a general review of his own theory. He believes that the action of heat as a cause of summer diarrhea is a direct one (it acts, that is, by a direct injury to the child); not an indirect one through the spoiling or bacterial infection of milk. This direct action may be either an acute heat disturbance, corresponding to a heat stroke in an adult; or a chronic injury of a very complex nature, through which the reaction of the child to injuries, such as those of artificial feeding, infection, etc., is changed. This action he compares to the general lowering of nutritional function observed in cases of parenteral infection; here, too, there may be many factors, such as lowering of the amount and ferment activity of the digestive juices, a lowered tolerance to all foods, a lowered resistance to all infections, or a secondary change in the intestinal flora. The temperature of the house, he reasserts, is all-important, as this may be far higher than the outdoor temperature. Very different clinical pictures may result from the interaction of different factors with heat. Spoiled milk he rejects as an important cause of summer diarrhea, on account of observations in which infants fed on bad milk but with other conditions favorable, developed no symptoms. That spoiled or infected milk causes diarrhea, is merely a theory, and so far absolutely lacks proof, he believes. He admits that dysentery may be transmitted in this way in epidemics, but considers this rare.

Schereschewsky⁹⁴ gives an excellent review of the literature on the relation of heat to infant mortality, with a very complete bibliography. His conclusions coincide, for the most part, with those of Rietschel. He believes, however, that a certain proportion of cases of summer diarrhea is due to specific infections, in the dissemination of which contact and flies are important. He lays great stress on the importance of good housing conditions and of rational hygienic care in the protection of infants against the dangers of hot weather.

Wolff⁹⁵ reports an interesting case which bears on Rietschel's theory that heat alone, without change in the feeding, may cause a diarrhea. A premature infant, fed on albumin milk, was accidentally overheated in an incubator, in which the bottles were too hot. The child's temperature rose to 42 C. and it had bad stools. On removal from the incubator and after a cool bath, the temperature fell to normal and the diarrhea ceased; the feeding had been continued unchanged throughout.

Zahorsky⁹⁶ finds no regional variation in the summer mortality of infants in different parts of the United States, except that a few western cities show remarkably low figures. He finds a higher mortality

in manufacturing cities. He has studied the relations between the mortality and heat curves in St. Louis for several summers and concludes that there is a relation between them which is more marked in spring than in the later summer. He has observed in many cases that very hot weather produces fever in infants; but he does not believe that it produces diarrhea, and believes that the evidence is against Rietschel's theory that the direct action of heat may cause diarrhea. In a foundlings' home under his care the summer mortality has greatly diminished since proper pasteurization and refrigeration of the milk has been instituted. He concludes that one of the chief causes of summer diarrhea is to be sought in the organisms whose virulence and activity may be increased. Bleyer⁹⁷ found no relation between humidity and infant mortality in the course of three summers in St. Louis. He has studied especially the relation between the "heat peaks" and the "mortality peaks" and finds a correspondence in only 22 per cent. of cases.

Knox⁹⁸ ascribes chief importance in the prevention of summer diarrhea to breast-feeding, feeding with pasteurized milk, and to sensible care of the infant.

The trend of opinion is, then, in regard to the summer hygiene of infants, to lay stress not only on the administration of milk of low bacterial count, but also on all measures to prevent overheating, such as very light clothing, frequent baths, and free circulation of air in houses.

NOTES ON ESPECIAL NUTRITIONAL DISTURBANCES

99. Hirschfeld: *Jahrb. f. Kinderh.*, 1913, lxxviii, Erg. H., 197.
100. Bauer: *Monatschr. f. Kinderh.*, 1913, xii, 510.
101. Hess: *AM. JOUR. DIS. CHILD.*, 1913, v, 298.
102. Helmholtz: *Jour. Am. Med. Assn.*, 1913, lxi, 2188.
103. Langstein: *Jahreskurs f. Aerztl. Fortbildg.*, 1913, iv, No. 6.
104. Frank: *Jahrb. f. Kinderh.*, 1913, lxxvii, 163, 333, 422.
105. Monti: *Wien. med. Wchnschr.*, 1913, lxi, 2262.
106. Frank and Stolte: *Jahrb. f. Kinderh.*, 1913, lxxviii, 167.
107. Clock: *Jour. Am. Med. Assn.*, 1913, lxi, 164.
108. Variot, Lavialle and Rousselot: *Bull. Soc. de Pédiat.*, 1913, xv, 337.
109. Sébilleau: *Revue Prat. d'Obstet. et de Gynec.*, 1913, xx.
110. Rosenhaupt: *Deutsch. Med. Wchnschr.*, 1913, xxxix, 752.
111. McClure: *AM. JOUR. DIS. CHILD.*, 1913, vii, 48.
112. Huldchinsky: *Ztschr. f. Kinderh.*, 1913, viii, 363.
113. Aschenheim: *Ztschr. f. Kinderh.*, 1913, viii, 161.
114. Brünig: *Arch. f. Kinderh.*, 1913, lx, 116.
115. Abt: *Jour. Am. Med. Assn.*, 1913, lxi, 1275.
116. Grulee: *Interstate Med. Jour.*, 1913, xx, 41.

Alimentary Intoxication

In intoxication the relation of the symptoms to those of disturbances of the vegetative nervous system has been studied.

Hirschfeld⁹⁹ has used Loewi's test in many cases of intoxication. In the normal individual one drop of one per mille epinephrin solution in the conjunctival sac will cause no mydriasis; in cases showing increase in the tonus of the sympathetic system a dilatation ensues. In ten cases of alimentary intoxication the test was positive. Among the 255 other cases examined, no condition gave the sign with any constancy. She concludes that an increase in the tonus of the sympathetic system is characteristic of alimentary intoxication.

Bauer¹⁰⁰ describes a distention of the lung observed in three cases of severe intoxication in infants, in two of which clinical diagnosis of the condition was proved at necropsy. He believes that this is fairly constant in intoxication, and that it predisposes to pneumonia. He draws attention to the resemblance of this condition to the distention of the lung seen in asthma and in animals after anaphylactic shock and peptone poisoning.

Hess¹⁰¹ has studied the pancreatic secretion of ten infants with acute intoxication, comparing it with that of three control cases with high fever. Material for examination he obtained by means of his duodenal catheter. He found a deficiency of lipase in the cases of intoxication, with a normal secretion of amylase and trypsin; these conditions were not present in the control cases. In cases of atrophy with a total increase in the amount of secretion he also found a diminution in lipase.

Helmholtz¹⁰² in cases of intoxication has used subcutaneous injections of 50 to 200 c.c. daily of a 6 per cent. solution of dextrose in Ringer's solution, on the principle that the dextrose can be used directly as a food. Among the twenty cases reported, not one showed sugar in the urine. Edema was seen rarely. The dietetic treatment was the usual one: tea or water for twelve to twenty-four hours, followed by small quantities of breast milk or albumin milk, which were gradually increased. The patients in the cases reported were, for the most part, in very poor condition on entrance. Advantages seen from the use of the solution were: improvement in the turgor of the skin, in the circulation, and in the mental condition, the coma disappearing more rapidly on this treatment.

Feer⁴⁷ believes that in intoxication albumin milk is sometimes even preferable to breast milk.

Ileocolitis

It has been shown that the etiology of ileocolitis, or "diarrhea from infectious origin" has been the subject of a great deal of study. As to the treatment there have also been many publications. The treatment advised by Kendall⁸⁰ and his coworkers has already been reviewed.

Most German writers believe that in this type of diarrhea alone albumin milk is ineffectual. Benfey (as above) states that Finkelstein, here also, has achieved good results with the food. Langstein¹⁰³ believes that no great advance has been made in the treatment of this condition. He has used albumin milk, also the buttermilk treatment recommended by Schaps, without success.

Frank¹⁰⁴ reports a series of seventy cases of "dysentery-like" diarrhea treated with whey. The cases showed, for the most part, blood and pus in the stools, and were, she believes, of an infectious origin in children already suffering from acute and chronic nutritional disturbances. She recommends the use of a combination of whey with cereal water. This food contains a high percentage of salt and very little carbohydrate; it is easily tolerated and marked losses in weight are prevented by the high salt content. She acknowledges that the treatment seems contradictory to the beliefs at present in force as to the damage caused by a high whey concentration; Feer's⁵⁸ observation, however, of its harmlessness in the absence of sugar and fat, and Langstein's of the same nature, would seem to explain this point. She warns against prolonged starvation in cases which have been fed on a diet rich in carbohydrates. In early cases she advises castor oil and rectal irrigation, with hunger for twenty-four hours, followed on the second day by five feedings of 50 gm. each whey and cereal water, increased on the third day. In mild cases milk may be added in small amounts at this time and gradually increased; in severe cases not till the fifth to eighth day. She warns against tannigen and tannismuth as they frequently induce vomiting, but gives bismuth subnitrate from the sixth to twelfth day. Full histories of the seventy cases are appended.

Monti¹⁰⁵ advises tannismuth in dysentery and infectious diarrhea.

Grulee¹¹⁶ has used a purely proteid diet in these cases with good effect; this consists of the curd of skimmed milk suspended in a 5 per cent. gelatin solution. Previously he used an arrowroot water as a diluent. This diet cannot be continued more than four days to a week. The gelatin water is gradually replaced by buttermilk, and the skimmed milk curds by those from whole milk, the diet then being albumin milk. He uses no drug except occasionally small doses of paregoric. He does not speak of any symptoms of sugar starvation arising on this diet; on theoretical grounds one would expect them.

Mehl-Nährschaden

The symptom complex known by this name has been described again at some length by Langstein.⁸ It is caused by an exclusive diet, long continued, of carbohydrates, and is marked by a hypertonic condition of the muscles, atrophy, and in one type of cases by edema.

Abt¹¹⁵ reviews the literature on this condition, and reports two cases of his own.

Frank and Stolte¹⁰⁶ have made chemical analyses of the liver in cases of this disturbance, and have found a decrease in dry substance and an increase in water as compared with analyses of the liver of control cases. They conclude that the disturbance leads to an increase in water throughout all the tissues, which explains the clinical fact of the very low resistance of these children to infection.

Lactic Acid Bacilli

Clock¹⁰⁷ reports the treatment of 117 cases of all forms of diarrhea with cultures of *B. lactis bulgaricus*. One or two tablets every two or three hours were given in mild cases; in severe ones two or three tablets at the same intervals. The diet varied; in most cases, the previous diet was continued; in some, starvation, followed with small amounts of boiled milk. Good results were shown by gain in weight and a rapid change in the nature of the stools. That this treatment should be successful in all forms alike of nutritional disturbance seems strikingly at variance with all theories in regard to their etiology. Kendall⁸⁰ has shown that in a certain group of infectious diarrheas, those caused by the gas bacillus, the administration of lactic acid bacilli is indicated. Further study and confirmation of Clock's results must be awaited.

Vomiting and Rumination

Variot, Lavalie and Rousselot¹⁰⁸ again recommend the administration of condensed milk with a very high percentage of sugar in cases of continued vomiting in infants. They ascribe its good effects to a change in the casein, making it resemble more closely that of breast milk.

Sébilleau¹⁰⁹ advises the administration in these cases of a tablespoonful of a 1.7 per cent. solution of sodium citrate before each feeding.

In nervous vomiting Rosenhaupt¹¹⁰ recommends anesthetizing the mucous membrane of the stomach. As cocain is too poisonous he advises the use of anaesthesin.

McClure¹¹¹ reports a case where nervous vomiting had reduced an infant to a state of extreme atrophy. Vomiting ceased at once when the child was given a semi-solid diet of one part farina, with six parts of whole milk; recovery ensued.

Rumination associated with uncontrollable vomiting was also successfully treated by Huldshinsky¹¹² with a similar semi-solid gruel.

Cases of rumination have been reported by Aschenheim¹¹³ and by Brünig.¹¹⁴

The Influence of Other Factors on Nutrition

117. Birk: Monatschr. f. Kinderh., 1913, xii, 1.

118. Miller: Arch. Pediat., 1913, xxx, 538.

The influence of psychic factors on the nutritional condition of infants has been suggested as a possibility by Czerny. An unfavorable psychic condition has been suggested as one factor in the condition of hospitalism. Birk¹¹⁷ reports two cases in proof of this theory. He believes that psychic stimulation and happiness are necessary for the nutritional well-being of the infant.

Theories as to the influence of teething are reviewed by Miller.¹¹⁸ The older writers ascribed many morbid symptoms to teething, while the modern tendency is to deny any connection between them. Miller takes a middle position, believing that in teething there is a reflex hypersensitiveness of the intestinal tract.

Anorexia

119. Tobler: Deutsch. med. Wchnschr., 1914, xl, 313.

The importance of anorexia as a symptom most often seen in disturbances secondary to parenteral infections, and also in young infants on the breast, and its treatment, as discussed by Langstein and Rosenstern, has already been reviewed. Rosenstern¹⁰ says that young infants on the bottle sometimes fail to take enough because the food is so much diluted that they cannot drink enough at one feeding if five feedings daily are given. He advises a temporary increase in the number of feedings to eight until the concentration of the food can be increased; then a return to five or six feedings may be made. He considers as another important factor in apparent anorexia, the marked air-swallowing shown by some infants. They stop sucking merely because the stomach feels too full. If such children are raised to a sitting position once or twice during feeding and are allowed to eructate swallowed air, they will afterward take more nourishment.

Tobler¹¹⁹ gives many practical points as to the treatment of anorexia; some of them are those already given above. He has seen little effect from radix gentianae luteae, which may be administered, as 3 to 6 drops of the "dialysat golaz" in sweetened water a quarter of an hour before feedings. Pepsin in the form of pepsin Grübler, 3 to 5 minims, ten minutes before feedings in combination with small quantities of dilute hydrochloric acid sometimes is effectual; theoretically its use seems irrational. One to 3 drams of Carlsbad or Vichy water ten minutes before meals has also been used. Feeding by gavage in young infants may tide over a dangerous period; in older infants it may be useful for its psychic effect and lead to an increased taking of food.

STERILIZATION OF MILK

- 120. Bradley: Arch. Pediat., 1913, xxx, 579.
- 121. Schlossman: Arch. f. Kinderh., 1913, lx-lxi, 676.
- 122. Grimmer: Monatschr. f. Kinderh., 1913, xii, 657.
- 123. Grimmer: Monatschr. f. Kinderh., 1913, xii, 1.

Opinions are still divided as to the importance to the infant of bacterial infection of milk. In the foregoing pages many opposing views have already been cited on this subject: Rietschel,⁹³ Bahrdt,²⁴ Zahorsky,⁹⁶ etc.

In accordance with the prevailing theories of the etiology of the nutritional disturbances, many German pediatricians minimize the importance to the child of bacterial contamination of milk, while those in America, for the most part, consider it of extreme importance.

Bradley¹²⁰ expresses the latter theory in an article on milk-poisoning. He believes that pasteurization is the best method of sterilization; and advises the process in which the temperature is held at 145 F. for thirty to forty-five minutes. Pasteurization may be easily carried out in the home by the following method: Five quarts of boiling water are set aside for ten minutes; then the milk bottles are set in the water and allowed to remain for forty-five minutes. He believes that milk obtained under proper precautions should not contain more than 10,000 bacteria per cubic centimeter.

Bahrdt²⁴ uses centrifuging as a means of purifying milk; he finds that the pathogenic bacteria can be removed in this way. Cream can not, however, be effectually purified in this manner, nor can milk during the hot months.

Grimmer^{122, 123} gives an extremely complete review of the literature for the past year on all subjects related to milk.

Schlossman¹²¹ writes of successful experiments with Lobeck's method of preparing milk free from bacteria.

BOILED MILK

- 124. Lane-Claypon: Ergebn. d. inn. Med. u. Kinderh., 1913, 635.
- 125. Coit: Arch. Pediat., 1913, xxx, 122.
- 126. Morse: Boston Med. and Surg. Jour., 1913, clxviii, 726.

Lane-Claypon has made an extensive investigation under the British Local Government Board on the effects of heated and super-heated milk on the infant's nutrition. This includes the report of animal experiments, made by different investigators; a report of clinical observations by various authorities on the effect of raw and boiled milk in hospitals; and a careful clinical dispensary investigation in which a series of normal breast-fed children was compared with one of normal children on boiled milk. The conclusions which she draws are these:

1. Additional proof is given that animals and infants develop better on milk of their own species.

2. Development of animals and infants on milk of their own species shows no difference whether the milk is raw or boiled.

3. On milk of a foreign species animals and infants develop slightly better if the milk is boiled.

4. It has by no means been proved that infants develop scurvy from boiled milk alone.

Coit¹²⁵ reviews the work of Lanc-Claypon and emphasizes its importance.

Morse^{126, 93} reviews the literature on boiled milk for the past year, also that on different methods of pasteurization of milk.

ROENTGEN RAY

127. Ladd: *AM. JOUR. DIS. CHILD.*, 1913, v, 345.

128. Ladd: *Arch. Pediat.*, 1913, xxx, 740.

129. Pisek and Lewald: *AM. JOUR. DIS. CHILD.*, 1913, vi, 232.

130. Major: *Ztschr. f. Kinderh.*, 1913, viii, 343.

131. De Buys: *AM. JOUR. DIS. CHILD.*, 1913, vi, 334.

Much work has been done on the Roentgen-ray examination of the infant stomach in normal cases and in those showing nutritional disturbances.

Pisek and Lewald¹²⁹ took series of Roentgen-ray pictures of the stomach of normal infants after a bismuth meal at intervals of ten minutes. They found no constant shape for the stomach; the shape apparently does not depend on the amount or character of the food taken, but on the amount of gas. They saw normally a rapid passage of food from the pylorus; in many cases food entered the duodenum one minute after its entrance into the stomach. They found that alkalies exercise a retarding influence on gastric motility; and that food, entering the stomach at different times, does not tend to mix.

Ladd^{127, 128} has written of gastric motility in the infant as studied by the Roentgen ray. He studied fourteen infants; to these he gave 2 drams of bismuth subcarbonate in their feeding. He finds, as do the other writers, an absence of peristalsis in the infant stomach; that some food passes into the duodenum immediately after the feeding is completed, and that the stomach is emptied of the larger amount in one and a half to two and a half hours. A considerable residue then remains for four and a half to seven and a half hours. The bismuth itself does not apparently affect the motility. The effect of different elements of food is studied, but no conclusions are drawn. A large amount of proteid seems to delay the emptying of the stomach, while a moderate amount of fat hastens it.

Major¹³⁰ used barium sulphate instead of bismuth. He believes that information regarding gastric motility cannot be gained when the former substance is used, for it adheres to the walls of the stomach, and gives it the appearance of being full, when in reality there is but a thin layer of barium over the mucous membrane. (He does not say whether the same criticism must be made of studies with bismuth.) His observations as to the normal shape of the stomach agree with those of the other authors. With the infant in a sitting posture he finds the most usual shape that of an inverted retort; in a recumbent position, that of an irregular sack. The gas bubble lies usually in the pyloric region, and is due, he believes, to swallowed air. The respiratory movements of the infant influence greatly the shape and position. Peristalsis is not so marked as in the adult. He too has seen food entering the duodenum immediately after the feeding. The time of complete emptying of the stomach, when no barium is used, is one and a half to two hours. He studied the stomach also in children with nutritional disturbances; in many cases of dyspepsia and in two cases of decomposition. He saw at times a delay in emptying, at times an increase in rate.

De Buys¹³¹ shows that the Roentgen ray may aid the diagnosis between spasm and stenosis in pyloric obstruction. In both, peristaltic waves may be seen. In spasm the stomach may lie in the normal position, and the food is slower to leave the stomach than in the normal case; in stenosis the stomach frequently lies to the left side, and the food leaves the stomach very slowly or not at all. Ladd,¹²⁷ in cases of pyloric stenosis saw peristalsis and a marked dilatation.

PYLORIC OBSTRUCTION

- 132. Koplik: *New York Med. Jour.*, 1913, xcvi, 57.
- 133. Hess: *Deutsch. med. Wchnschr.*, 1913, xxxix, 412.
- 134. Hess: *AM. JOUR. DIS. CHILD.*, 1913, v, 268.
- 135. Hess: *Post Graduate*, 1913, xxviii, 556.
- 136. Hess: *Ztschr. f. Kinderh.*, 1913, ix, 19.
- 137. Putzig: *Therap. Monatschr.*, 1913, xxvii, 25.
- 138. Richter: *Jour. Am. Med. Assn.*, 1914, lxii, 353.
- 139. Keefe: *Am. Jour. Obstetr.*, 1913, lxvii, 383.
- 140. Ibrahim: *Jahrb. f. Kinderh.*, 1913, lxxvii, 199.
- 141. Strauch: *Med. Rec.*, New York, 1913, lxxxiv, 386.
- 142. Ramstedt: *Ztschr. f. Chirurg.*, 1912.

The writings on this subject have this year been extremely numerous; many, however, are merely reports of cases.

Koplik distinguishes three groups in cases of obstruction:

1. Pure spasm without a palpable tumor mass, but with explosive vomiting, visible peristalsis and a marked loss in weight.
2. Pylorospasm accompanied by a relative stenosis.
3. Typical hypertrophic stenosis.

He reports ten cases which healed without operative treatment; he makes the observation that peristaltic waves may be observed for a long time during convalescence. He says that the duodenal catheter of Hess may be useful but cannot always be introduced.

Hess^{133, 134, 135} has written several articles on the use of his duodenal catheter in the treatment and diagnosis of pyloric obstruction. He has also used the tube to obtain duodenal contents for examination of the digestive ferments in normal and abnormal children and for bacteriological examination, and in the study of the cases of congenital obstruction of the bile ducts.

Putzig¹³⁷ reports favorably on a case treated with the duodenal catheter, and gives data as to the technic to be used.

As to the operative treatment, much has been written. Richter¹³⁸ reports 22 cases of pyloric obstruction in which operation was performed, with a mortality of 13 per cent. In nineteen of these cases the obstruction was due to stenosis, in three to spasm. A tumor mass was palpated in all but one of these cases previous to operation. In nineteen the operation was a posterior gastro-enterostomy. He believes that in the diagnosis, the Roentgen ray cannot be entirely relied on, as bismuth will pass through the opening even in stenosis.

Keefe¹³⁹ reports cases treated surgically; Ibrahim,¹⁴⁰ Strauch¹⁴¹ and many others, cases recovering on medical treatment.

The operation of Ramstedt^{136, 142} has been much discussed, but the posterior gastro-enterostomy continues to be the most popular in America.

DUODENAL ULCERS

143. Holt: *AM. JOUR. DIS. CHILD.*, 1913, vi, 381.

144. Schmidt: *Berl. klin. Wchnschr.*, 1913, i, 593.

The reports of ninety-one cases of duodenal ulcers in infancy has been reviewed by Holt, who adds four cases of his own. From these he concludes that in the etiology atrophy is the most important predisposing cause. Seventy per cent. of the cases occurred between 6 weeks and 5 months. The ulcers were nearly all situated above the papilla, and showed macroscopically a punched-out appearance; microscopically, an absence of round-cell infiltration. As to the symptoms, in one-third of the cases there were none attributable to the ulcer. Hemorrhage was the only definite symptom; blood in the stools of an atrophic child in the absence of a diarrhea should suggest an ulcer, Holt believes. Collapse, with a concealed hemorrhage, occurred in a certain number of cases. As to diagnosis, he recommends the passage of a duodenal catheter. In one case of his own the presence of blood

in the eye of the tube established the diagnosis. He believes that the danger from this procedure is slight.

Schmidt¹⁴⁴ believes that duodenal ulcer is more common in infancy than has been thought. He found it post mortem in 18 per cent. of a very large number of necropsies on infants. He believes that not only atrophy but all general wasting diseases predispose to ulcer.

122 South Michigan Avenue.

REVIEW OF SYPHILIS WITH ESPECIAL RELATION TO HEREDITARY SYPHILIS *

HARVEY PARKER TOWLE, M.D.

BOSTON

Part Two — Newer Therapy

The foundation on which the newer therapy of syphilis rests is composed, in largest part, of material derived from the results of the serum tests which we have just been considering in Part One. It follows that, as the solidarity of a structure is affected by the strength or weakness of its foundations, so must the opinions expressed in Part Two for and against salvarsan and neosalvarsan be judged in accordance with the estimates formed of the strength or weakness of the serum tests.

CRITICISMS

Having seen that criticism of the serum test method exists, it cannot occasion surprise that the newer therapy of syphilis should also be criticized. Klotz⁶⁷ is most outspoken in his objection to an employment of salvarsan or neosalvarsan as a routine method of treatment of syphilis. He admits that, occasionally, the newer remedies do possess a certain value, but, speaking generally, the indications for their use will be reduced to a minimum if mercury and iodids are prescribed with proper judgment and administered with thoroughness. Gaucher⁴⁷ uses the Ehrlich remedies as a last resort, i. e., when mercury has failed. He considers them both untrustworthy and dangerous. Hoffman⁵⁹ states that, if we may judge the efficiency of the newer therapy by its success in protecting the offspring of syphilitic unions, we are not yet justified in abandoning the ancient rule of forbidding syphilitics to marry until they have been under observation for at least three years. The most that we are permitted to hope from the new remedies is that we shall be able to substitute two or three injections of salvarsan for five or six courses of mercury. Experience leads Levy-Bing and Duroeux⁷³ to write that they cannot recommend the new remedies as the best method of treatment in hereditary syphilis. Müller⁹⁰ is in doubt as to which method is superior, mercury or salvarsan. Langford⁷⁰ favors mercury when there is visceral involvement. Noeggarath⁹⁴ considers mercury

* This is a continuation of the abstract article appearing in April. The references will be found at the end of the first article.

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superior to salvarsan if the infant's physical condition is not good, or if a septic process exists, even one not syphilitic. Watrazewski¹³⁰ much prefers mercury to salvarsan. Shields¹⁰⁸ was so disappointed with the results of salvarsan that he doubts if it can either abort or cure. Nichols and Mutot⁹² call salvarsan a useful adjunct to mercury. Wilson¹³⁴ opposes the routine employment of salvarsan and neosalvarsan. The present popularity he ascribes to a lamentable international hysteria, the result of "an over-riding of science by commercialism." He warns the profession that unless it takes a saner view of the uses and limitations of the new remedies, five or ten years hence every child born of syphilitic parents will inherit the disease.

De Aja replies that the criticisms prove only that the critic lacks the courage to use the remedies as they should be used. If he would only give them in adequate doses, his opposition would disappear at once. De Azua,⁶ Dreyfus^{33, 34} and Iverson⁵⁷ agree with de Aja that such insufficient dosage cannot be expected to give proper results. Spiethoff¹¹³ even declares that if the total dosage is too small, salvarsan is dangerous, but that the same reproach cannot be made if adequately large. Whitehouse and Clark¹³³ are so enthusiastic over salvarsan therapy that they assert that a disease which salvarsan does not at least relieve cannot be syphilis.

METHODS

Almkvist⁵ says that, in his opinion, a combination of salvarsan and mercury is the best method of treatment. He reasons that the cure of syphilis is produced by the continuous action of substances on the spirochetes. Salvarsan cannot exert such an effect for, acting in the blood-stream, it does not reach the spirochetes hidden in the tissues. Mercury used alone cannot cure for the reason that it is impossible to give it in sufficiently large amounts without doing damage to the patient. Therefore, the only logical method is to reinforce the action of salvarsan by the supplemental effect of mercury. Barduzzi¹⁰ says that, without mercury, salvarsan is powerless to cure. According to de Azua,⁶ frequent injections are necessary if salvarsan is not supplemented by mercury. Corbus²⁷ believes that it is possible to cure with either salvarsan or mercury alone, but a quicker result is obtained if they are used in combination. Fordyce,⁴² Mortimer⁸⁷ and Morton⁸⁹ advocate the combined method, the last because he doubts the effectiveness of salvarsan therapy. Nicholas and Mutot⁹² always give salvarsan in combination with mercury. Eisenstaedt³⁵ and de Favento³⁸ get better results when the drugs are used together. Gougerot and Parent⁴⁹ say that it is immaterial which of several approved methods is chosen

provided the scheme of treatment adopted includes daily injections of some soluble mercurial salt.

Dreyfus³³ concluded that salvarsan is most effective when a total of 5 or 6 gm. is injected within six or eight weeks and followed by a course of mercurial inunctions.

Gardner⁴⁶ quotes Schreiber as advocating the administration of a total amount of 6 gm. divided into four doses and one dose injected every other day. It is to be noticed, however, that, in a more recent paper Schreiber¹¹⁰ advises the very different procedure of an initial dose not to exceed 0.3-0.4 gm., and, instead of every other day, subsequent injections once in two weeks. Schreiber explains his changed attitude on the ground that he has come to the conclusion that the customary dose in Germany is too large and that the too frequent repetition predisposes to undesirable cumulative action. Iverson,⁶⁹ following Schreiber's earlier method, gives one injection every other day up to the number of four. Four, McDonagh⁸² thinks, is the smallest number of salvarsan injections which is likely to cure. Lueders⁷⁶ reports that, to relieve deafness, he had to give six injections of salvarsan in the course of ten weeks in order to secure the result.

Gardner⁴⁶ found 1.5 gm. in 20 c.c. water a satisfactory dose of neo-salvarsan. McIntosh and Parker⁸⁴ injected 0.6 gm. in a solution of 150 c.c. of bacteria-free distilled water. In the primary stage they give two initial doses, with a third after three weeks. In the secondary stage, they first inject three doses and, after an interval of eight weeks, a fourth. Tertiaries they treat by an injection every two or three months until the W. R. becomes negative. Stühler¹¹⁸ advises doses of neosalvarsan of not over 0.4-0.6, repeated at intervals of ten days.

Scholtz and Riebes¹⁰⁹ have adopted as a routine method two successive injections of 0.4-0.5 gm. of salvarsan within twenty-four hours, followed by daily inunctions of mercury for three or four weeks together with a subcutaneous injection of mercury once every five to eight days. Then, they repeat the series for a second time. They report that, by using this method, they have had but one accident in 1,200 cases and neurorecurrences have been eliminated. They also report that they have recently given three successive injections of 0.4-0.5 gm. of salvarsan within a period of twenty-four hours with no untoward result. Marshalko and Veszpremi⁸⁹ do not think such large amounts of salvarsan are necessary, as smaller doses are just as effective and likewise safer. It is interesting to read in this connection that Szametz¹²¹ obtained a brilliant result in a case of chorea from a dose of only 0.2 gm. of salvarsan. Wechselmann¹³¹ urges giving smaller doses of salvarsan than is customary at the present time. Spiethoff,¹¹³ on the other hand, states that if salvarsan is to be used at all, at least

in secondary syphilis, the dose should certainly not be small. He would follow salvarsan with mercury in order to prevent recurrence.

Müller⁹⁹ states that intramuscular injections of salvarsan produce more lasting effects than intravenous.

Gruenberg⁵² prefers salvarsan to neosalvarsan when it is desired to try to abort the disease, to treat secondary cases, to give large doses or frequent injections or to obtain a rapid effect. Whitehouse and Clark,¹³³ from one or more injections of salvarsan, obtain the same effects as with four or more injections of neosalvarsan.

The newer remedies do not protect the offspring from his syphilitic parents much more effectually than the older (Hoffman⁵⁹). The children of the next five or ten years will be subjects of inherited syphilis if the present blind confidence in salvarsan and neosalvarsan continues (Wilson¹³⁴). Experience does not commend the Ehrlich remedies as the best treatment for inherited syphilis (Levy-Bing and Duroeux⁷³). It is a question whether the newer therapy is more efficient than the older (Müller⁹⁰). The administration of salvarsan was followed by death in two cases of hereditary syphilis (King-Smith⁶⁶). Salvarsan is more dangerous in the presence of visceral, inherited syphilis (Langford⁷⁰). While Ehrlich's warning that salvarsan should not be used in infants has received little support in fact, nevertheless, it is true that poor physical condition and septic disease of any origin constitute contraindications to its employment (Noeggarath⁹⁴). Salvarsan should never be used under any condition for the deafness of hereditary syphilis (Beck¹¹). Salvarsan may be used in such cases, but, probably, better after mercury (Voorhees¹²⁷). Only the future can prove that large doses of salvarsan in concentrated solutions are really as harmless as they seem and alone can teach us in which forms of the inherited disease salvarsan is not to be used (Noeggarath⁹⁴). Although he obtained the result in two of his nine cases, Welde¹³⁸ is impressed by the obstinate resistance which the positive serum reaction of hereditary syphilis offers to the injections.

Opinions differ as to the value of the new remedies in the special manifestations of inherited syphilis. In interstitial keratitis, general opinion is not favorable to them. Post¹⁰¹ reports that his results were good. In the hereditary syphilis of bones, skin and mucous membranes, Langford⁷⁰ found salvarsan, as a rule, less efficient than mercury. In the exceptional cases, resistant to mercury, salvarsan was more efficient. Steiger¹¹⁴ was well pleased with salvarsan in hereditary syphilis when given intramuscularly in the form of a 40 per cent. suspension in iodopin. Swift and Ellis¹¹⁹ were impressed by the results from the administration of the milk of salvarsanized mothers to nurslings. On the other hand, King-Smith⁶⁶ was unfavorably impressed.

HEREDITARY SYPHILIS AND DOSAGE

The literature contains very little concerning the most effective dose of the newer remedies in the treatment of inherited syphilis. Noeggarath⁹⁴ estimates that, in syphilis of children, the initial dose should correspond to 0.0002 gm. salvarsan per each kilo of body weight. Succeeding doses should be gradually increased in amount until they reach 0.1 gm. per kilo of body weight. King-Smith⁶⁶ likewise advises beginning with small doses and increasing the size gradually. Compared to adults, children bear relatively large doses of salvarsan (King-Smith⁶⁶) and of mercury if the liver and kidneys functionate perfectly (Levy-Bing and Duroeux⁷³).

Ordinarily, salvarsan is, as in adults, injected intravenously. The choice of a vein for the operation differs with the preference of the individual operator. Some use the veins of the head. King-Smith⁶⁶ prefers the jugular vein. Weil, Morel and Moriquand¹³² tried, experimentally, rectal injections. Somewhat to their surprise, they found that children bore rectal injections well if a little laudanum was added to the salvarsan solution. The disappearance of the visible signs of the disease proved that, contrary to the experience in adults, the drug was, in children, actually absorbed from the rectum. Neither local nor systemic reactions occurred.

ACTION OF SALVARSAN AS SHOWN BY THE URINE

Hitherto, we have considered the action and effect of salvarsan and neosalvarsan only from the clinician's point of view. There have been published, however, reports showing that attempts have been made to secure evidence from other sources. Capelli²¹ thinks that his investigations of the nitrogen excretion by the kidneys demonstrates that salvarsan is a disturber of metabolic processes. Capelli found the nitrogen output was increased (2 gm.) for twenty-four hours after an intravenous injection of salvarsan notwithstanding a decrease in the nitrogen intake of 6 gm. After twenty-four hours, the nitrogen excretion fell to 1.8 gm. below the ingestion. The excretion urea was perceptibly reduced. Capelli attributes the primary increase to a "Herxheimer reaction" and the presence of a slight fever. His final conclusion is that salvarsan alters the metabolism in syphilitic subjects, producing a temporary increase and a subsequent, more lasting decrease in the excretion of nitrogen. Greven,⁵¹ using a so-called "biological method," reported that salvarsan could be detected in the urine within an hour after its injection. He found evidence of its continued presence for fourteen days after subcutaneous injections and for seventeen to eighteen days after intramuscular. He thought that mercury hin-

dered excretion while the iodids favored. Lorenz⁷⁵ found arsenic in the urine one-half hour after an intravenous injection of salvarsan. Twenty-eight to fifty-seven hours later he could discover only a slight trace.

SALVARSAN IN THE BLOOD

Scholtz and Riebes¹⁰⁹ failed to discover a trace of salvarsan in the blood-serum four to six hours after the injection.

SALVARSAN AND THE CEREBROSPINAL FLUID

Lorenz⁷⁵ found that the lymphocytosis and increased globulin content in the cerebrospinal fluid was reduced by salvarsan. Levy-Bing, Duroeux and Dogny⁷¹ report that there occurs, after salvarsan, a true hypertension of the cerebrospinal fluid which is always accompanied by an increase in the amount of albumen. They do not doubt that salvarsan causes meningeal reactions more frequently than mercury.

SALVARSAN AND BLOOD-PRESSURE

In twelve cases of mental disease, McKinnes⁸³ could not demonstrate that salvarsan increased the blood-pressure even when given in so large a volume as 195 c.c. of the solution.

LETHAL DOSE

Merian, Girauld and Duret⁸⁵ endeavored to determine the fatal dose of the two substances in rabbits. The lethal level of neosalvarsan was approximately in the proportion of 0.42 gm. per kilo body weight. The toxic dose varied from 0.14 gm. upward. With salvarsan, the lethal level was reached at 0.10 gm. per kilo body weight.

CAUSE OF THE SALVARSAN REACTIONS

Marshalko and Veszpremi⁸⁰ do not believe that the so-called "water-error" plays any part in the production of the systemic symptoms of reaction after salvarsan. Nobl and Peller⁹³ could not demonstrate the bacterial contamination of the solution to be a cause of the fever. They doubted also if the fever after salvarsan was due to circulating endotoxins. They concluded that the more recent the generalization of the systemic symptoms of syphilis and the larger the relative dose of salvarsan, the greater was the febrile reaction. Wachenfield¹²⁹ considers it still remains to be proved that salvarsan reactions are due either to the solvent, to bacteria or to bacterial toxins.

Schreiber¹¹⁰ suggests that the untoward symptoms which occur after injections of salvarsan and neosalvarsan may be due to a species of anaphylaxis. Plausibility is lent to the idea by Swift's success in

reproducing the symptoms of anaphylaxis in guinea-pigs by means of repeated injections of salvarsan. In this connection it is not to be forgotten that Gradwohl's⁵⁰ explanation of the luetin reaction was that it was a phenomenon of anaphylaxis. Stühmer¹¹⁸ ascribes the salvarsan reactions to "auto-anaphylaxis," a state especially favored by certain conditions such as, for example, the increased susceptibility of the auto-intoxication of pregnancy.

De Aja¹ has observed that immediate and late reactions after salvarsan injections occur more frequently in cases in the secondary stage of syphilis. De Azua⁶ agrees that the secondary stage favors relapse. Nicholas and Mutot⁹² and Gruenberg⁵² have seen neurorecurrences develop in cases of secondary syphilis in spite of energetic treatment. Rimini¹⁰⁷ is convinced that the secondary cases offer a peculiarly stubborn resistance to curative treatment.

It is an accepted fact that the secondary stage of syphilis yields the greatest percentage of positive results to the serum test. The writers just quoted assert that the greatest frequency of neurorecurrences is in secondary syphilis. The question is unavoidable, What is the connection between these facts?

DEATHS AFTER SALVARSAN

Several fatal cases have been reported during the past year, one by de Favento,³⁸ one by Keyes,⁶⁵ three by Hirsh⁵⁷ (of which one case was his own and two Hammer's), two of hereditary syphilis by King-Smith,⁶⁶ one by Newmark⁹¹ and one by Marshalko and Veszpremi.⁵⁰

The number of salvarsan injections is in the thousands. The fatalities can almost be reckoned in single figures. Nevertheless, it is not disputed that a certain small number of patients have died under circumstances which threw suspicion on the injected remedy as the cause. The partisans of salvarsan maintain that the remedial substance should not be held responsible, but preexisting forces with which it has no connection except in so far as it may have acted as the exciting agent which stimulated these forces into fatal activity. The opponents declare that the direct cause of death is the toxic action of salvarsan. To the ordinary reader the conclusion would seemingly be unavoidable that occasionally salvarsan is the cause of death, perhaps directly, perhaps indirectly.

AUTOPSY EVIDENCE

Marshalko and Veszpremi⁵⁰ concluded that, in their case, changes found at the autopsy pointed to the fact that the fatal encephalitis was caused by the toxin action of the salvarsan. They could find no actual signs of inflammation, but only multiple hemorrhages into the brain from stasis or thrombosis without any changes of especial significance

in the substance of the brain. De Faventa³⁸ thinks that the bacterial contamination of the solvent was the cause of the findings in his fatal case. Newmark⁹¹ reports the autopsy of a patient dying after an intramuscular injection of 0.3 gm. salvarsan into each buttock in which a softening of the cord was present.

NEURORECURRENCE

As ordinarily used, neurorecurrence refers to the symptoms which develop in some part of the nervous system after a considerable time has elapsed since the last treatment. The question of the comparative frequency of the condition after salvarsan and neosalvarsan and after mercury and the iodids has been sufficiently discussed above. The theories of the relationship of the action of the remedial substances to the development of the symptoms of neurorecurrence demand more attention. Some say that they are the direct result of the toxic action of the drugs. Some say that they are not the result of toxicity, but of insufficient dosage; that the symptoms are not to be attributed directly to the action of the remedies themselves, but to the latent foci of disease which they have accidentally stimulated into action.

Wechselmann¹³¹ considers neosalvarsan more neurotropic than salvarsan, and at the same time, clinically and serologically less active. De Aja¹ thinks salvarsan is less able to prevent neurorecurrences than is mercury. Ellis³⁶ denies that salvarsan in any way predisposes to these nervous relapses. Fordyce⁴² has never had a case of neurorecurrence in the auditory nerve after salvarsan. Gardner⁴⁶ thinks there is no choice between salvarsan and neosalvarsan so far as relapses are concerned. Gruenberg⁵² considers the effects of neosalvarsan more cumulative and more toxic than of salvarsan. Kall⁶² believes neosalvarsan is the more neurotropic and, in ambulatory, the more dangerous. Mortimer⁸⁷ does not think it is proved that salvarsan harms the nervous system. Müller⁹⁰ reports that, in 200 salvarsan cases, 7.5 per cent. of the patients developed symptoms of neurorecurrence within seven to twelve weeks. Dreyfus^{33, 34} states that neurorecurrences have become more frequent since the introduction of salvarsan. Ravaut¹⁰³ says that, in the presence of spirochetes salvarsan is neurotropic, that is, predisposes to affections of the nerves. Whereas, under ordinary conditions, without salvarsan, syphilis causes a meningeal reaction in 67 per cent. of all cases, after salvarsan medication, the figures are raised to 87 per cent. He therefore concludes that salvarsan should be used with caution if the cerebrospinal fluid shows signs of meningeal reaction. Spiethoff¹¹³ agrees that since the introduction of salvarsan, neurorecurrences have become more frequent, not, however, because of the salvarsan, *per se*, but because of the timidity of the operator.

Schreiber,¹¹⁰ once the advocate of high dosage, now believes that the massive and frequent doses customary in Germany are dangerous. Marshalko and Veszpremi,⁸⁰ from the autopsy evidence of their fatal case, conclude that salvarsan is safer in small doses. Nobl and Peller⁹³ say that salvarsan is toxic. Wolff and Melzer¹³⁰ concluded that neosalvarsan is more toxic than salvarsan. Gruenberg⁵² thinks neosalvarsan the less toxic and its effect the less cumulative. Kall⁶² belongs to the group of those who, advocating one, refer incidentally to the toxic properties of both. He advocates salvarsan on the ground that it is *less* dangerous and *less* neurotropic than neosalvarsan. Noeggarath⁹⁴ wonders what the future will show is the effect of concentrated solutions injected intravenously. Levy-Bing and Duroeux⁷³ say that the symptoms of toxicity are largely dependent on the functional perfection of the liver and kidneys. Rimini¹⁰⁷ declares that the symptoms of neurorecurrence which follow after salvarsan are due to the lighting up, by the injections, of old foci of disease. Mortimer⁸⁷ also attributes the symptoms of nervous involvement to the reawakening of a previous luetic process, possibly an accumulation in the nerve tissue of spirochetes which have escaped destruction (Müller).⁹⁰

DOSE AND NEURORECURRENCE

De Aja¹ says that it is not the salvarsan to which neurorecurrence is due, but to the use of too small an amount to prevent the event. Almkvist³ argues that if it were only borne in mind that it is necessary to sterilize the organism to prevent neurorecurrences, more frequent injections would be given. De Azua⁶ proportions the frequency of repetition to the urgency of the case. Ravaut¹⁰³ once wrote that the likelihood of neurorecurrence went hand in hand with the frequency of the injections (the dosage). Dreyfus,³³ replying to Ravaut's later paper,¹⁰³ does not deny the accuracy of Ravaut's observations, but says that they are based on the results of a too timorous use of the remedy. Spiethoff¹¹³ states that neurorecurrences occur in inverse ratio to the intensity of the salvarsan therapy. Iverson⁶⁰ declares that, rather than favoring neurorecurrence, high doses of salvarsan are preventative. Scholtz and Riebes¹⁰⁹ concur.

AUDITORY SYMPTOMS OF NEURORECURRENCE AND SALVARSAN

Rimini¹⁰⁷ reports eight cases of hereditary syphilis in which the auditory symptoms of neurorecurrence seemed to have been the direct result of salvarsan medication. Not one patient had ear symptoms before salvarsan. One to three months after the injections all had developed symptoms of aural disease. According to J. C. Beck,¹² the symptoms of neurorecurrence in the ear may appear at any time from

two to eight months after the salvarsan. As salvarsan may possibly predispose to the conditions, Beck thinks it inadvisable to give it to hereditary syphilitics with symptoms of aural involvement or to adults whose ear symptoms have developed within six to eight weeks of a previous injection. Biggs¹³ reports a case in which deafness developed within forty-eight hours after salvarsan was injected. Carpenter²³ thinks that salvarsan is least effective in the treatment of syphilitic affections of the organs of special sense.

THE EYE

In the diagnosis of hereditary syphilis, the ocular manifestations of the disease have a peculiar importance. One result of the Ehrlich remedies has been to give us a more accurate conception of the changes which hereditary syphilis produces in the eye. Many symptoms which earlier were attributed to the deleterious effect of salvarsan medication have been shown by recent careful study to have resulted from pre-existing syphilitic processes and not from the action of the remedy.

Stiern has drawn from statistics the conclusion that only one-half of all syphilitic fetuses are born alive, and that 80 per cent. of the living half develop some form of ocular syphilis, most often an interstitial keratitis. Neumann is said to have found that 81.9 per cent. of the syphilitic infants in his clinic had symptoms of iritis. Oscar Dodd³² estimated that, of every 5,000 cases of all forms of eye disease, one will be a manifestation of syphilis which, in 1 or 2 per cent. of the total, is some form of disease of the orbit. He says, the primary manifestation may be either an involvement of the orbital margin, a periorbitis or a gumma of the orbital wall. The prognosis is worse in hereditary syphilis than in the acquired form.

The eye symptoms indicative of involvement of the central nervous system are even more serious. According to Knapp,⁶⁸ if it is desired to avoid irreparable damage, the symptoms must not escape immediate recognition. In the diagnosis of ocular syphilis, Knapp found the W. R. of inestimable value. Monradian⁸⁸ thinks its value in these cases is doubtful.

Otchaposky's results from the salvarsan treatment of ocular syphilis were disappointing, which is contrary to Post's experience. Of the 120 cases reported by Otchaposky, only forty-five showed any improvement. He even saw the other eye attacked while treatment was in progress. His best results were obtained in iritis, although, at that, the best were not so good as with mercury and the iodids. Relapses were more frequent. Reese¹⁰³ considers that salvarsan is an indispensable adjunct to mercury in the treatment of ocular syphilis without, however, being able to replace mercury.

NEURORECURRENCE; SITES OF PREDILECTION

Returning to the general subject of neurorecurrence, the fact is at once interesting and suggestive that when its symptoms develop after treatment, they seem to exhibit a distinct tendency to limitation to some one nerve trunk and that certain nerves seem to be particularly susceptible. Thus, de Aja² says that a very large majority of the cases of relapse affect one of three nerves which, in order of frequency, are the facial, the acoustic and the trigeminal. Fully 50 per cent., he says, occur in the facial nerve and are peculiarly obstinate to treatment compared to the ease with which other nerve systems respond.

DO SALVARSAN AND NEOSALVARSAN CURE?

A committee once met to consider how patients afflicted with syphilis might be cared for most efficiently. In the course of the discussion the question was raised as to whether a specialist in syphilis was to be preferred to a general practitioner. A physician of more than ordinary attainments rose and stated as his opinion that the care of the syphilitic to-day is not the intricate and complex problem of a few years ago which a specialist alone could handle. Then we had nothing to guide us but clinical experience. To-day, our position is different. With means of testing the blood at command, the detection of the disease is assured. By injections of salvarsan, its cure is easy.

The climax of the speech is in the last three words, "cure is easy." Whether we shall agree or disagree with the speaker, depends on our interpretation of the discussion of salvarsan and neosalvarsan in Part Two and of the serum test in Part One.

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PRIMARY PULMONARY ACTINOMYCOSIS IN A CHILD AGED TEN

WITH POST-MORTEM EXAMINATION *

FRANCIS HUBER, M.D., AND SAMUEL BERKOWITZ, M.D.
NEW YORK

Actinomycosis pulmonis as a primary condition, though uncommon in America, has been observed rather frequently abroad. In the German literature Aschoff, Heuser, Rutinmeyer, Köster, and Kashiwanuva report such cases in detail, the latter describing four instances, while Lindt described a single case of primary involvement of the apices. In America, case reports of only a very limited number of this type have been recorded, owing perhaps, to a great extent, to the relative infrequency of the various types of this ailment. The disease may be acute or chronic, local or general. The symptoms vary within wide limits; they may be pronounced or, on the other hand, indefinite.

Actinomycosis, as we know, is an infectious disease caused by a specific micro-organism, *Actinomyces bovis*, originally named "ray fungus" by Bollinger and Hartz. It must not be confounded with the so-called pseudotuberculosis, streptothrix or cladothrix infections or atypical actinomycotic processes described by J. H. Wright under the name of "nocardioses."

It was first recognized in man by Langenbeck in 1845, who described a case of vertebral caries—the pus containing numerous "sulphur-like" granules. Twelve years later, in 1857, a patient with thoracic involvement was reported by Lebert. Murphy of Chicago, in 1883, was the first clinician on this side to report a patient suffering with this disease. The identity of the human and bovine disease was first pointed out by Ponfick. In a masterly monograph, Israel, in 1885, proved that the disease was transmissible from man to animal. The experiments proved that the infection could be transmitted from man to rabbits. These observations were later confirmed by Ponfick, Wolff, Hanan, John and Boström. Hodenpyl (1890) deserves the credit of having reported the first case of pulmonary actinomycosis in America.

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The organism is widely distributed in nature and is easily isolated from certain grasses. Direct contagion is denied by many, though a few cases have been reported in which men have contracted it from animals. At the Royal Victoria Hospital one of the earliest cases occurred in the nurse attending a case of actinomycosis.

The infection may take place as follows: through (*a*) the mouth and pharynx, (*b*) the respiratory tract, (*c*) the gastro-intestinal tract, (*d*) the skin and wounds, and (*e*) idiopathically (?).

Pathologically, two types of lesions are recognized as characteristic of this disease, that is, (1) neoplastic and (2) inflammatory. Each type has selective tendencies in the special species chosen. Horses and cattle suffer more frequently from the former and man and hogs from the latter. The neoplastic type usually occurs in very vascular tissues and clinically resembles sarcomatous invasions, which may, however, result in spontaneous recovery. The inflammatory type which is most frequently seen in man, usually avoids parenchyma, spreads rapidly and forms characteristic sinuses from which the sulphur-like granules are discharged and can be shown microscopically to contain the "rays." Microscopically the actinomycotic area lends itself to division into three zones; from within outward they are: (*a*) the central zone of fungi and detritus, (*b*) the middle zone of round and epithelial cells which supplies the inner with detritus, and (*c*) the outer zone of granulation tissue.

The bacteriology is of especial interest to the laboratory worker, and although it is deserving of more than a passing remark, space does not permit any extensive references.¹

The severity, location and type of the infection determines the nature of the symptoms. The sites are the following in their order of frequency: (1) cervical-facial, 55 per cent., (2) thoracic, 20 per cent., (3) abdominal, 20 per cent., of which more than half (50 to 60 per cent.) involve the cecum, and (4) cutaneous, 5 per cent. In the thoracic form definite signs and symptoms are usually absent until the disease is far advanced. Cough, with fetid sputum, consolidation and cavity formation may appear late, with attending cachexia, anemia and temperature of a variable type. The presence of an inflammatory swelling or a board-like induration of the thoracic wall is suggestive; later on suppurating foci or sinuses may result and arouse our suspicions as to the real nature of the process, which may be confirmed by a microscopic examination of the pus. Pulmonary cases, it has been asserted, are usually secondary to the abdominal variety. Because

1. For a full description of the micro-organisms of actinomycosis, the reader is referred to Wright, J. H.: *Biology of the Micro-organisms of Actinomycosis*, Jour. Med. Research, new series, 1905, viii, 349.

of the involvement of the right lower lobe in the majority of the cases it is thought that the lymphatic channels are to a great extent responsible for the transmission of the infection from the right side of the abdomen to this region. Infection through the blood-stream, however, seems more logical together with "*locus resistantiae minoris*" as in other infections, particularly so when the lung has been exposed to trauma.

The exact diagnosis can be readily established in many instances by microscopic recognition of the fungi from the sulphur-like bodies found in most cases. It is necessary that these granules be examined in thin preparations to avoid error—the liability "to look but to see not." Translucent bodies are positive evidences of such involvement, especially if club-shaped.

The prognosis, according to McKenty, varies with the extent, severity, and location—the nearer the surface or within the scope of radical surgical interference, the greater the possibility of early and successful cure. Therefore, it is evident, as this writer states, that cervical infections give a more favorable prognosis and are fatal in only 11 per cent. of cases, while on the other hand the abdominal mortality ranges as high as 71 per cent. and the thoracic even higher—83 per cent.

Treatment of actinomycosis is symptomatic and consists in the administration of potassium iodid continued over a long period of time. The drug appears, however, to act less favorably in the pulmonary type. The surgical treatment of this variety has not given brilliant results. The Roentgen ray is of doubtful value. Vaccine treatment has given some success after a considerable period.

CASE-REPORT

History.—J. B., a schoolboy, aged 10, of Italian parentage, was admitted to the Beth Israel Hospital (Dr. Huber's service), June 18, 1913, in a drowsy and restless condition, speaking only at times, always incoherently. The following history was obtained with difficulty through an interpreter. It was not until some time later that we learned that the boy was in the habit of spending much of his time in a stable.

Present Illness.—About four weeks before admission the child was struck on the chest by a man, with sufficient force to give rise to considerable soreness of the right side and pain, causing him to complain for a few days. Two weeks later he was suddenly seized with high fever, headache, anorexia, prostration, and vomiting, the latter continuing for three days after the onset. On the fourth day of the illness an unproductive cough developed and was soon followed by a thin brownish expectoration which afterward became greenish and fetid, and was later accompanied by dyspnea. Three days before admission he began to show evidences of restlessness, drowsiness and incoherence, which have been increasing.

Previous History.—The previous history of the patient may be summarized in the following few remarks. "Instruments" were necessary at his birth. He was breast-fed until one year of age. His habits were always good. He was never sick before. The family history is without importance.

Physical Examination.—The patient appeared fairly well developed and nourished. Marked dyspnea, great prostration and extreme facial pallor were observed immediately on approaching his bed, together with a disagreeable fetid odor which pervaded that section of the ward. The skin was warm and dry. Eye examinations were negative. Extensive herpes labialis was present. The tongue was thick and coated, brownish white, and the pharynx was congested. The teeth appeared normal.

Thorax: Since, in the history, the chief complaints centered in the respiratory apparatus, the thorax and its contents received particular attention. The movements of the right chest-wall were greatly diminished during both acts of respiration. There was marked induration of the anterior and lateral aspects of the right side of the chest, particularly below. Though the regions involved felt hard, there was no evidence of local inflammation, no redness, no tenderness, increased local heat or deep-seated fluctuation. The interspaces were more prominent on the opposite side. Percussion over the affected side gave a



Fig. 1.—Pulmonary actinomycosis, showing extensive involvement of right side.

“boardy” note which was diminished from above downward. The breath-sounds were very distant and bronchial in character, heard best after coughing. The voice and whisper sounds were also of this type. Fine and large moist râles accompanied the breath-sounds. These physical signs extended to the lower lobes but also diminished in intensity. Over the whole left lung there were areas of compensatory exaggeration of the normal findings together with scattered portions of bronchial breathing and fine moist râles.

Examination of the heart showed it to be in the normal position.

Abdomen: The right lobe of the liver was pushed down about an inch below the costal margin; otherwise the findings here were normal.

Course.—On admission to the hospital, the patient's temperature was 103.6 F. It continued remittent, ranging from 101 to 105, with a corresponding increase in the pulse-rate. The respirations varied from thirty to fifty per minute.

The blood examination showed 12,000 leukocytes with 84 per cent. polynuclears and 16 per cent. mononuclears (150 cells counted). Four days later a second blood count gave 9,200 leukocytes with 79 per cent. polynuclears and 21 per cent. mononuclears (the second count was made after the thoracotomy). Therefore, during a period of four days, the patient's infection was becoming exceedingly severe and his resistance poorer.

The urinalyses were negative.

A roentgenogram disclosed a dense white shadow occupying the upper three-fourths of the right pulmonary field, which was interpreted as fluid—perhaps a lung abscess or a sacculated empyema.

Many specimens of sputum were examined microscopically by the members of the medical staff, but no "ray fungi" were found. (Lebedeff, Machinskii, and Sokoloff mention cases which were diagnosed from the sputum findings.) The reports in each instance in our case showed polynuclear leukocytes, elastic tissue, streptococci, and staphylococci. Macroscopically the sputum was greenish yellow, thick, semisolid, tenacious, and foul-smelling. The odor was characteristic of gangrene of the lung and accordingly the case was regarded as extensive pulmonary gangrene, the cause of which was not evident.

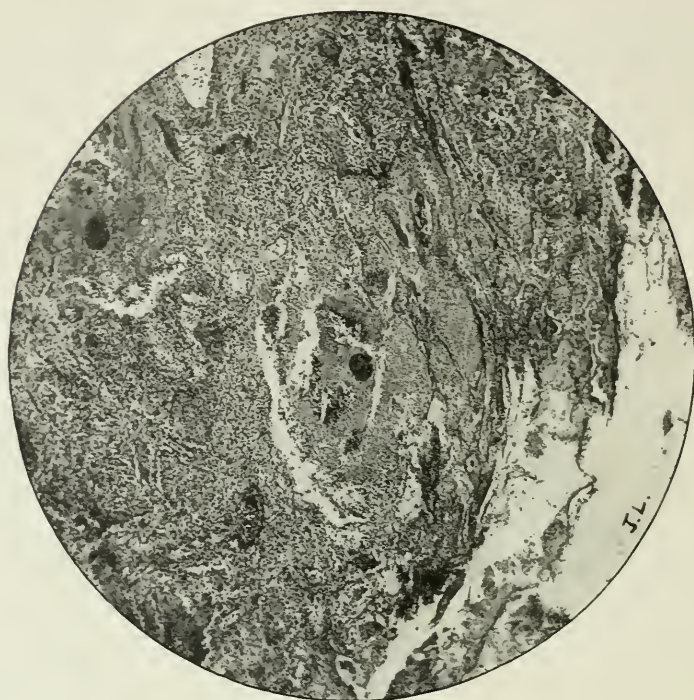
Operative Procedures.—In view of the physical signs, clinical course, and roentgenographic findings, the chest was aspirated in the sixth right interspace in the midaxillary line. After several attempts with needles of increasing caliber, 8 c.c. of creamy greenish yellow, tenacious and very foul-smelling pus were evacuated. This was later reported on fresh smear examination to contain staphylococci and Gram-positive diplococci. Culturally there was no growth but some anaerobic bacteria were present.

The thoracotomy, preceded by an exploratory aspiration, the needle being left *in situ* as a guide, was performed the same evening under nitrous oxid and oxygen anesthesia. The site chosen was in the same area from which the pus had been previously obtained. A pint of thick creamy pus was slowly evacuated. The work had to be done rapidly as the condition of the patient even while on the operating-table, was precarious. A large rubber tube was quickly inserted, the dressing applied and the child taken to the ward.

His condition continued serious with attacks of restlessness, delirium and stupor lasting a week, the patient dying from toxic paralyzes and exhaustion.

The history of trauma to the chest and the obscure etiology of the pulmonary gangrene in an apparently well-developed boy aroused great interest; there was also a strong suspicion that external violence had been a contributory factor. The condition was therefore reported to the coroner's office in the hope that we might perhaps get an opportunity through necropsy to ascertain, if possible, the cause of this illness. A post-mortem examination was performed by Dr. Otto Schultz, who, after having seen gross sections of the gangrenous right lung, suggested the possibility of actinomycosis; but not until a thorough search for other foci was made (an important point in the opinion of McKenty), did he consider the disease as of primary origin in the lungs. The diagnosis was later corroborated by stained microscopic sections. A detailed gross pathologic report of the condition in the lungs follows:

Necropsy Findings.—The right upper lobe is very large and completely solid. Its pleura is thickened and covered everywhere with fresh fibrin. On cross-section this lobe is almost completely gangrenous, green, and honeycombed with abscesses containing yellowish-green pus, the largest of them being the size of a hen's egg. These abscesses are not encapsulated, but are lined by dirty irregular shreds of lung tissue. The lower lobe is studded with numerous patches of bronchopneumonia and from the center of the majority of these patches small amounts of pus can on pressure be forced out. The remainder of the lung is solid with reddish-gray hepatization. The left lung is covered with a thin layer of fibrin on its outer surface. This, on section, shows numerous patches of red



Figs. 2 and 3.—Actinomycosis pulmonis (primary).

hepatization which are wide-spread. The bronchial lymph-nodes are larger and softer than normal.

The microscopic examination by Dr. Eli Moschcowitz, pathologist to the Beth Israel Hospital, gives the following condensed report:

The pulmonary alveoli are completely filled with exudate, in part consisting of almost pure fibrin and in part with fibrin and large round mononuclear cells. Scattered throughout the consolidated lung are discrete darker areas which under low power resemble miliary abscesses. These areas vary in size from the head of a pin to a millet-seed and consist of collections of small round cells in the center of which are "ray fungi" varying in number from one to a dozen. The lung tissue in these areas is absent, the wall consisting of partially destroyed consolidated alveoli. The exudate immediately surrounding the "ray fungi" is completely necrotic. The walls of the lung alveoli are normal. The pleura is covered by a thin layer of hyalinized fibrin.

In reviewing rather hastily the more recent literature, we find the disease to be rare in children. In McKenty's series of thirty-seven cases seen in America (nine in females) occurring within 100 miles of Montreal, the youngest patient was a boy, aged 10. The incubation period varies from a few days in the cases occurring in the jaw to weeks and months in the abdominal and pulmonary varieties. It has been found, as a result of observation and experiments, that infection does not occur unless there is a lesion in the skin or mucous membrane.

Foulerton lays stress on the fact that, in many cases, an exact diagnosis on clinical evidence is impossible until the chest or abdominal walls are involved by extension of the process outward. Perforation of the skin then occurs and the organism may be discovered in the secretions on microscopic examination.

Incidentally we may refer to the disappointment in not being able to find or isolate the organism in the sputum or other secretions in some instances. The difficulties in the positive identification of the parasite by laboratory methods may be due to several causes: in the first place there is extreme difficulty of obtaining growth of many parasites of this class on artificial mediums, and, secondly, because of the varying morphology at different phases of the life-cycle of the parasite, recognition is not easy. It is well known that the mycelial or "ray-fungus" form represents only one of the three forms in which the parasite occurs. The typical mycelium and the mycelium in the earlier stages of "fragmentation" when it is breaking up into "rod forms," represent the only stage at which the parasite can be recognized positively by the microscope. At a later stage when sporulation has occurred, the irregular "bacillary" form and spherical spores resembling the pus cocci are seen, both staining deeply by the Gram method.

CASEIN IN INFANT-FEEDING

THE PREPARATION OF DRY POWDERED PARACASEIN AND PRELIMINARY
EXPERIMENTS CONCERNING ITS USE AS THE PRINCIPAL
PROTEIN CONSTITUENT IN INFANT FOOD *

A. W. BOSWORTH, A.M., AND HENRY I. BOWDITCH, M.D.
GENEVA, N. Y. BOSTON

WITH THE ASSISTANCE OF
B. H. RAGLE, A.B.

In a previous communication¹ we mentioned the preparation of dry powdered paracasein and showed that it was completely digested when fed as a constituent of infant food. It seems desirable to give the details of the method used in preparing this substance, together with additional experiments involving its use.

I. METHOD OF PREPARING DRY POWDERED PARACASEIN

Fat-free milk is curdled by the addition of rennin and when the curd has become so firm that it will make a clean break when the finger is thrust diagonally into it and then lifted up, divide it into small pieces, remove the whey and wash several times with water. If the curd is obtained from a dairy, or for any reason becomes matted together, it must be broken up and then passed through a meat chopper.

The finely divided curd is now placed in a large vessel such as a cheese vat or a clean wash tub, and to it is added five volumes of water for every volume of milk used to produce the curd. The curd is now dissolved by adding about 10 c.c. of concentrated ammonia water for each quart of milk used. As the curd goes into solution rather slowly, more or less continuous agitation will be necessary.

After complete solution the paracasein is precipitated in the following manner: Take 2.5 c.c. of glacial acetic acid for every quart of milk used and dilute it with 25 volumes of water. Add this diluted acid to the solution of paracasein, a few cubic centimeters at a time,

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* The expense of this investigation was defrayed by the Boston Floating Hospital, Boston, Mass. The chemical work was done in the Biochemical Laboratory of the Harvard Medical School, Boston, Mass. We wish to thank Dr. Otto Folin for his courtesy in extending this privilege to us.

1. Bowditch, H. I., and Bosworth, A. W.: *AM. JOUR. DIS. CHILD.*, 1913, vi, 394.

and with constant agitation. This addition of acid will precipitate the paracasein and very close attention is required at this point, for an excess of acid will redissolve the precipitated paracasein which should separate out as a large flocculent precipitate quickly settling to the bottom of the vessel. If a very fine precipitate is formed, which does not settle rapidly, it is an insoluble calcium salt of paracasein² and the addition of a little more acid will change it to the desired form, free paracasein. More or less acid than the amount specified may be required to give the proper precipitate, depending on the condition and age of both the milk and the curd and on the amount of ammonia used to dissolve the curd. After the paracasein has settled and the supernatant liquid has been removed, it is washed several times with water and then redissolved, using the same volume of water as before, but using caution at this point so that an excess of ammonia is not added, for this would cause hydrolysis with consequent loss in yield of paracasein. It is best to dilute the ammonia water with fifty volumes of water and use just enough of this diluted ammonia to dissolve the paracasein. After complete solution the paracasein is again precipitated with dilute acetic acid and washed as before.

The procedure from this point on depends on how pure a product is desired. At each precipitation some insoluble calcium paracaseinate is formed and carried down with the large mass of free paracasein and it is only by repeated precipitations that the calcium is all removed. In order to secure practically ash-free paracasein it will be necessary to make six or seven precipitations.² Two precipitations, if properly made, will give a fairly good product.

After the final precipitation and washing the paracasein is placed in a linen bag and allowed to drain for two hours. It is then transferred to a mortar and triturated with 95 per cent. alcohol. After allowing to settle, decant off the alcohol and again triturate with a fresh portion of alcohol, repeating two or three times. The dehydration is completed by allowing the paracasein to remain in contact with a large volume of 95 per cent. alcohol for an hour or two. This alcohol is removed by decantation and filtering through the linen bag and if desired the bag and its contents may be placed in a press to remove most of the remaining alcohol. The preparation is now made to pass through a 20-mesh sieve and finally dried at a temperature between 80 and 90 C.

With proper care as to technic the final product will be a fine powder. If a powder is not obtained it can be secured by grinding in a coffee mill. If grinding is necessary the material should be placed in

2. Van Slyke and Bosworth: *Jour. Biol. Chem.*, 1913, xiv, 203.

the drying oven again in order to remove any alcohol which might be held inside the larger particles.

One product made by us with two precipitations contained 1.7 per cent. moisture, 0.4 per cent. ash and 98 per cent. paracasein. It was insoluble in water, slightly soluble in a 5 per cent. solution of sodium chlorid and completely and quickly dissolved by a dilute solution of sodium carbonate. The substance prepared in this manner is paracasein, not casein. The only difference between paracasein and casein is in the size of the molecule. One molecule of casein is split, by rennin, into two molecules of paracasein and no other substance is produced as was formerly believed.³ This is quite similar to the production of two molecules of dextrose from one molecule of maltose.

II. THE USE OF DRY POWDERED PARACASEIN AS THE PRINCIPAL PROTEIN CONSTITUENT OF INFANT FOOD

1. *Low protein feeding.*—As we wished to secure additional data on the digestibility of dry powdered paracasein and also learn to what extent it might be used to supply the protein in infant food, we secured the data given below. The child selected for this experiment was 8 months old, weighed 4,480 grams and was in good physical condition. He had been receiving 1,470 c.c. each twenty-four hours, of the following mixture:

Sixteen per cent. cream.....	160 c.c.
Buttermilk	800 c.c.
Sterile water	640 c.c.
Milk-sugar	53 gm.

A study of his nitrogen metabolism was made during four days while he was receiving this food and the figures given in Table 1 under the heading "Buttermilk Period," are averages representing the average figures for a twenty-four-hour period. The food was then changed to one made according to the following formula:

Sixteen per cent. cream.....	161 c.c.
Distilled water	1,439 c.c.
Lactose	89 gm.
Paracasein	25 gm.

It will be noticed that the mineral constituents in the last formula are supplied by the whey carried in the 161 c.c. of 16 per cent. cream. We will call attention to this point in another paper, simply stating here that the low sodium chlorid excretion while the child was on this food was due to the small mineral intake.

The protein in the above formula is not all paracasein for 161 c.c. of 16 per cent. cream will contain about 4 gm. of protein of which 2.8 gm. will be casein and 1.2 gm. albumin. The 2.8 gm. of casein

3. Bosworth: Jour. Biol. Chem., 1913, xv, 231.

is equivalent to an equal amount of paracasein, so that out of the 29 gm. of protein in the formula all but 1.2 gm. can be considered paracasein. Just what favorable influence this 1.2 gm. of albumin might have on the utilization of the paracasein we are unable to state at this time.

The child took the food well after the first few feedings and seemed to maintain his general good condition during the nine days he received it. The nitrogen metabolism while on this food is represented by the figures in Table 1 under the heading "Paracasein Period." These are average figures for a twenty-four-hour period.

TABLE 1.—LOW PROTEIN FEEDING. URINE ANALYSIS; AVERAGE FIGURES FOR TWENTY-FOUR-HOUR PERIODS

	Buttermilk Period	Paracasein Period
Volume in c.c.	832.0	1110.0
Total acidity as N/10	128.4	46.9
P ₂ O ₅ , gm.	1.002	0.395
Chlorids as NaCl, gm.	1.100	0.165
Total nitrogen, gm.	2.020	1.335
N as NH ₃ , gm.	0.311	0.205
N as urea, gm.	1.544	0.782
Uric acid, gm.	0.073	0.056
Creatinin, gm.	0.020	0.020
Creatin, gm.	0.028	0.025
Nitrogen in feces, gm.	0.365	0.173
Gain in weight per twenty-four hours.....	41.2	13.3

A study of Table 1 indicates no marked change in the general nitrogen metabolism with the change of food and no toxic effect was observed. It will be noticed that the amount of nitrogen in the feces during the paracasein period is less than half that found during the buttermilk period, indicating better digestion and absorption of the paracasein. The average daily increase in body weight during the paracasein period was less than during the buttermilk period. The low phosphorus and chlorin eliminations during this period would indicate that this was due to a lack of sufficient inorganic material in the food. We hope to publish work on this before long.

2. *High protein feeding.*—It occurred to us that the dry, powdered paracasein might be combined with whey, or milk, and cream to make preparations quite similar to Finkelstein's formula. We made several experiments along this line and will report two of them here because they seem to possess special significance. One child was fed a high protein food containing plenty of whey and the other child a

high protein food containing an extremely small amount of whey. The two formulae are as follows, each being a twenty-four-hour quantity:

Formula 1.—Fat, 1.5 per cent.; sugar, 6 per cent.; protein	$\frac{.25 \text{ whey}}{6.5 \text{ dry casein}}$
Twenty per cent. lactose solution.....	337 c.c.
Thirty-two per cent. cream.....	44 c.c.
Whey	355 c.c.
Water	662 c.c.
Lime-water	21 c.c.
Paracasein	93.0 gm.

Formula 2.—Fat, 1 per cent.; sugar, 6 per cent.; protein	$\frac{0.4 \text{ whey}}{6.5 \text{ dry casein}}$
Twenty per cent. lactose solution.....	384 c.c.
Thirty-two per cent. cream.....	68 c.c.
Water	967 c.c.
Paracasein	96.0 gm.

In each case a study of the nitrogen metabolism was made during a preliminary period on a "normal" diet and also during the period of paracasein feeding. In no case was all the paracasein indicated in the formula ingested during a twenty-four-hour period, for it was quite impossible to manipulate the feeding-bottle so that the infants received all the paracasein; more or less always remained adhering to the walls of the bottle. The figures for total nitrogen in the urine, however, indicate the ingestion of large amounts of protein. The urines were collected in twenty-four-hour quantities and the analytical data obtained are given in Tables 2 and 3.

CLINICAL REPORT (RÉSUMÉ)

Experiment 1 (High Protein and Whey).—A male child 7 months old weighing 11 pounds 1 ounce. Diagnosis, rachitis, otitis media chronica. His digestion was normal and he was gaining weight. With the administration of special formula no untoward effect was seen until the last day or so, when diarrhea set in. The child's disposition and general condition remained good. He took his food fairly well. Although calorically feeding 120 calories per kilo, he lost during the experiment 9 ounces. (Unfortunately he died ten days later of bronchopneumonia.)

Experiment 2 (High Protein and Very Small Amount of Whey).—A male child 7 months old weighing 13 pounds, 13½ ounces. Diagnosis, normal child and feeding; well developed and nourished. This patient took his food well at all times, showed but little regurgitation and no indigestion nor diarrhea. There was no fever at any time. Although getting 120 calories per kilo he lost 1 pound in seven days during the experiment. (This patient was discharged well.)

The high protein feeding resulted in a greatly increased elimination of ammonia in both cases. In Table 3 the creatin figures are fairly constant, while in Table 2 quite a marked change is noticed in the creatin excretion with the beginning of the high protein period. We are unable to suggest any explanation for this.

TABLE 2.—HIGH PROTEIN FEEDING WITH ABUNDANCE OF WHEY
URINE ANALYSIS

Twenty-Four- Hour Period Ending	Body Weight, lbs.	Volume, c.c.	Specific Gravity	Total Acidity as N/10	Chlorids as NaCl, gm.	Total N, gm.	N as NH ₃ , gm.	Uric Acid, gm.	Cre- atinin, gm.	Creatin, gm.
August 3	540	1.007	*	0.434	2.147	*	0.0864	0.0210	0.0454
August 4	500	1.005	48.0	0.684	1.624	0.328	0.0603	0.0216	0.0313
August 10 ...	11½	270	1.013	*	0.210	1.663	*	0.0951	0.0150	0.0095
August 11	510	1.015	*	0.410	5.483	*	0.0704	0.0180	0.0069
August 12	620	1.015	38.4	0.149	5.034	0.521	0.0992	0.0190	0.0064
August 13	560	1.018	39.2	0.320	5.457	0.533	0.1066	0.0218	0.0049
August 14	430	1.015	*	0.189	5.058	*	0.0813	0.0164	0.0054
August 15	650	1.018	6.5	0.286	7.826	0.874	0.0819	0.0188	0.0100
August 16 ...	10½	620	1.017	3.7	0.355	8.575	0.868	0.0174	0.0061
August 17	600	1.017	8.467	0.622	0.0212	0.0072

* Alkaline.

TABLE 3.—HIGH PROTEIN FEEDING WITH SMALL AMOUNT OF WHEY
URINE ANALYSIS

Twenty-Four- Hour Period Ending	Body Weight, lbs.	Volume, c.c.	Specific Gravity	Total Acidity as N/10	Chlorids as NaCl, gm.	Total N, gm.	N as NH ₃ , gm.	Uric Acid, gm.	Cre- atinin, gm.	Creatin, gm.
August 1	420	1.008	52.9	0.341	1.705	0.219	0.0643	0.0200	0.0130
August 2	520	1.005	54.4	0.327	0.895	0.267	0.0688	0.0208	0.0169
August 10 ...	13 lbs., 13½ oz.	950	1.008	79.8	0.794	6.118	0.798	0.0950	0.0241	0.0186
August 11	960	1.014	61.4	0.483	8.602	1.317	0.0658	0.0230	0.0121
August 12	800	1.016	89.6	0.378	8.823	0.560	0.1240	0.0240	0.0192
August 13	840	1.015	67.2	0.091	7.762	0.592	0.1091	0.0247	0.0220
August 14	730	1.018	29.2	0.000	9.403	1.226	0.0898	0.0234	0.0167
August 15	530	1.020	63.6	0.091	9.834	0.564	0.1219	0.0225	0.0151
August 16 ...	12 lbs., 13½ oz.	630	1.017	44.1	0.025	7.444	0.494	0.0209	0.0175

In Table 3 on August 14 it will be noticed that the urine was chlorin-free, chlorin appearing in the next twenty-four-hour specimen. This appearance of chlorin-free urine was not accompanied by symptoms of any kind.

The most surprising feature of these experiments in high protein feeding was the fact that no toxic or other unfavorable condition was manifested by the child receiving the small amount of whey. The extremely small amount of whey in the formula used for this experiment would lead one to expect the appearance of some such condition as that noticed by Holt, Levene, et al.,⁴ when they fed their high protein "synthetic" food. The non-appearance, in our experiments, of the symptoms noted by them would suggest that some constituent other than the protein was responsible for the results obtained by them; possibly the 250 c.c. of tenth-normal sodium hydroxid (equal to 1 gm. NaOH) used to dissolve the curd, a constituent of their high protein "synthetic" food.

SUMMARY

1. A method is given for preparing dry powdered paracasein for use in infant-feeding.

2. It is shown that this paracasein is very easily digested and absorbed, and judging from the elimination of creatinin and creatin, it seems possible to maintain normal nitrogen metabolism by its use in infant-feeding.

3. It is shown that disturbances (fever, toxic symptoms, etc.) do not result from feeding this paracasein in exceptionally large quantities for seven days, even if fed with only the small amount of whey carried in 68 c.c. of 32 per cent. cream.

4. Holt, Levene et al.: *AM. JOUR. DIS. CHILD.*, 1912, iv, 265.

THE PRESENCE OF LACTIC ACID IN THE URINE IN CYCLIC VOMITING OF CHILDHOOD*

FRANK P. UNDERHILL AND H. MERRIAM STEELE, M.D.
NEW HAVEN, CONN.

Although the etiology of recurrent or periodic vomiting of children has been attributed to a variety of abnormal conditions none of the numerous theories advanced offers an adequate explanation for the cause of the symptoms observed.¹ The more recent ideas tend to correlate recurrent vomiting with some defects in metabolic processes, notably those concerned with carbohydrate transformations. Thus, in the pathologic state under discussion, diacetic acid and acetone in the urine are particularly prominent as abnormal constituents of that excretion. Inasmuch as carbohydrate deficiency in inanition in childhood leads rapidly to the same urinary findings, one may query with a great deal of pertinence whether these compounds mentioned can be regarded as factors in the etiology of cyclic vomiting, for they may indicate merely the effect of withdrawal of food, especially carbohydrates.

The purpose of the present communication is to report a case of cyclic vomiting showing one feature hitherto unrecognized, namely, the presence of lactic acid in the urine.

History.—The subject, a boy aged $2\frac{1}{2}$ years, had been visited by one of us (Steele) at intervals since he was 3 months old. He had had several attacks of vomiting at irregular periods accompanied by a temperature ranging from 100 to 104 F. Up to the period of vomiting for which the urinary findings are presented below the child had been well fed, and attempts, which were partially successful, were made during the period of the attack to maintain a carbohydrate-rich diet. We therefore feel convinced that complete inanition did not play a significant rôle in the present instance. January 20 vomiting commenced, with a temperature of 104 F. at 10 a. m. The physical examination was negative. Calomel was given with good results. The temperature at night rose to 106 F. January 21 the bowels were loose and the temperature was 98.8 F. The child was apparently in normal condition on January 22. The twenty-four-hour specimens of urine were subjected to the analyses indicated in the accompanying table, the usual methods employed in this laboratory being followed.

*From the Sheffield Laboratory of Physiological Chemistry, Yale University, New Haven, Conn.

*Submitted for publication, April 10, 1914.

1. Sedgwick: See AM. JOUR. DIS. CHILD., 1913, ii, 209, where the literature is reviewed.

Lactic acid was isolated as the zinc salt, according to the well-known method.² The salt was identified by a determination of the water of crystallization and the content of zinc oxid. From the twenty-four-hour specimen of January 20 more than 0.56 gm. zinc lactate was obtained.

Calculated for	$\text{Zn}(\text{C}_3\text{H}_5\text{O}_2)_2 + 2\text{H}_2\text{O}$ Per Cent.	Found, Per Cent.
H_2O	12.9	12.7
ZnO	33.33	33.43

At intervals between attacks of vomiting lactic acid was absent from the urine.

TABLE SHOWING URINE ANALYSIS DUR—

Date, Jan. 1913	Volume, c.c.	Specific Gravity	Reaction to Litmus	Total N., Gm.	NH_3 N., Gm.
20	600	1.020	Acid	6.30	0.13
21	600	1.020	Acid	5.54	0.14
22	620	1.015	Acid	5.20	0.20

In addition to lactic acid, diacetic acid, acetone and protein were present in the urine of January 20, all gradually disappearing as the attack passed off. An unusual feature in the present case is the presence in the urine of significant quantities of acid bodies—diacetic and lactic acids—without an appreciable rise in ammonia excretion. Ordinarily increased acid elimination is accompanied by augmented ammonia output, since ammonia is employed by the organism as a neutralizing agent. It is therefore evident that in our case some alkali other than ammonia must have been used for this purpose.

The significance of lactic acid in the urine is not well understood, although its presence in the urine in eclampsia,³ pernicious vomiting of pregnancy,⁴ phosphorus poisoning,⁵ etc., is well known and its appearance may probably be taken as an indication of disturbed carbohydrate metabolism either induced by the pathological state itself or as a result of an accompanying inanition. Its meaning with respect to the etiology of recurrent vomiting of childhood must be left, therefore, for future investigation.

2. Hoppe-Seyler-Thierfelder: Handbuch der chemische Analyse, Ed. 7, p. 449.

3. Zweifel: Arch f. Gynäkol., 1905, lxxvi, 537.

4. Underhill: Jour. Biol. Chem., 1906-07, ii, 485.

5. Mandel and Lusk: See Am. Jour. Physiol., 1906, xvi, 129, for literature.

From the table it will be noted that creatin was present throughout the period of observation. In the intervals between attacks it was also a constant constituent of the urine, being present to the extent of 30 to 50 mg. creatin per 100 c.c. of urine. As the work of Rose,⁶ Folin⁷ and Krause⁸ has demonstrated, creatin is normally present in the urine of young children and it is therefore unnecessary to connect it in any way with the etiology of cyclic vomiting.¹ An increased elimination during an interval of attack with its usual accompanying inanition may be explained on the hypothesis of carbohydrate withdrawal.⁹

—ING AN ATTACK CYCLIC VOMITING

Creatinin, Mg.	Creatin, Mg.	Protein	Diacetic Acid and Acetone	Indican	Rotation Ventzke Degrees
210	102	Positive	Positive	Trace	—1.5
486	324	Trace	Trace	Trace	—0.6
176	177	Negative	Negative	Trace	0.0

6. Rose: Jour. Biol. Chem., 1911, x, 265.

7. Folin: Jour. Biol. Chem., 1912, xi, 253.

8. Krause: Quart. Jour. Physiol., 1913, viii, 87.

9. Graham and Poulton: Proc. Royal Soc., London (B) 1914, lxxxvii, 205.

These authors have recently criticized severely all estimations of creatin in urines containing diacetic acid.

445 Orange Street—226 Church Street.

A CLINICAL STUDY OF TYPHOID FEVER IN CHILDREN *

HENRY DWIGHT CHAPIN, M.D.
NEW YORK

The fact that children have not been supposed to be very susceptible to typhoid fever, and, when affected, are apt to exhibit an irregular type of the disease, would seem to render a study of cases of value for future comparison and reference. It is during an epidemic that they are most liable to be attacked, so that such an occasion affords the most favorable opportunity for a study of any peculiarities the disease may show in early life. Since the employment of Widal's test, the field has widened by proving that typhoid fever in certain mild types may be overlooked in children or mistaken for some other affection.

During the fall of 1913, an epidemic of typhoid fever occurred in the lower East side of New York, including 521 reported cases, with a mortality of 11.7 per cent. Many children were attacked as shown by the following reported number of cases: Under five, 36; five to nine, 98; ten to fourteen, 87. These cases, I think, show a much larger proportion of attacks among children than have usually been reported. A little over two-fifths of all the cases in this epidemic occurred in children under 14 years of age. Dr. Osler in reporting on 1,500 cases of typhoid fever in Johns Hopkins Hospital states that 231 were under 15 years. Dr. Ogan of the New York Health Department, in a study of 1,500 cases in 1912, to compare with Osler's series, found 437 under 15 years. In a personal communication to the writer, Dr. Ogan states that children under 12 constitute one-quarter of the population of New York City and that approximately one-quarter of all cases of typhoid fever occur under 12 years, so that children contribute their fair ratio to this disease. It is evident that we must revise our ideas as to the frequency with which typhoid fever occurs in children.

The cases occurred during August, September, October and November and the Board of Health succeeded in tracing the outbreak to infected milk. It was found that 10 per cent. of the people living in the district were supplied by one milk company and that 70 per cent. of the cases reported were getting milk from one dairy. A case of typhoid fever was found in the vicinity of this dairy, although not

* Submitted for publication, June 8, 1914.

* Read before the American Pediatric Society at Stockbridge, Mass., May 26, 1914.

directly connected with it, and it is highly probable that the infection was carried by flies. When the milk from this source of supply was cut off by the Health Department, the epidemic ceased. The fact of it being a milk outbreak probably accounts for the large number of children attacked.

The eleven cases here reported were treated in the children's wards of the New York Postgraduate Hospital. The ages were as follows: 2 years, 1 case; 3 years, 2 cases; 4 years, 2 cases; 5 years, 2 cases; 6 years, 3 cases; 7 years, 1 case.

The duration of the fever, including the period before admission, as given in the histories, was varied and ran, from the shortest to the longest period, as follows: 7 days; 11 days; 16 days; 18 days; 19 days (two cases); 20 days; 21 days; 24 days; 33 days; 42 days. In only five cases did the temperature run very high during the active stage, two reaching 106 F., one 105.2 F. and two ranging from 104 F. to 105 F. The temperatures were not high in the other cases and were distinctly remittent toward the close of the disease. The diagnosis was confirmed in every instance by a positive Widal and no case showed any rose spots.

A study of the blood on admission is shown in the following table:

TABLE 1.—RESULTS OF BLOOD EXAMINATION ON ADMISSION

Age Years	Reds	Whites	Polymor- phonuclears Per Cent.	Lympho- cytes Per Cent.
8	5,200,000	7,200	58	42
5	4,028,000	5,700	65	35
3½	4,352,000	10,000	81	18
4	4,088,000	4,200	52	48
2	4,130,000	9,100	68	32
3	4,270,000	13,700	68	32
6	4,848,000	9,200	82	16
6	4,600,000	7,400	64	36
4	4,800,000	10,100	74	26
6	4,264,000	8,700	79	21
5	4,600,000	6,000	64	35

An inspection of this table shows the red corpuscles to be about normal in numbers. There is no appreciable diminution of the leukocytes except in one case, a child of 4 years, in whom they numbered only 4,200. These cases thus failed to show the leukopenia that is supposed to accompany typhoid fever. In the differential count, a study of the polynuclears shows what may be considered a polynucleosis when we have in mind the age of the patients. In every instance the percentage is appreciably higher than the average for the age. The two most marked were in a 3-year-old child showing 81

per cent. against a normal of 42 per cent., and a child of 6 years with 82 per cent. against a normal of 52 per cent.

The lymphocyte count was more irregular, being normal in only one case, a child of 6 years, with 36 per cent. In two cases, the count was above the normal for the age, one child of 8 years giving 42 per cent. against 33 per cent. average, and another of 4 years showing 48 per cent. against 41 per cent. average. The remaining eight were below the normal for the age. In two of the cases the relative diminution was very marked, one child of 3 years having only 18 per cent. and another of 6 years 16 per cent. against 47 per cent. and 37 per cent. averages for these ages.

A study of the urine showed that the kidneys were not much affected in this series; six cases were entirely negative, three gave traces of albumen, with occasional hyaline and granular casts, and a small number of pus cells were also reported in four of the cases.

The gastro-intestinal symptoms were neither marked nor severe. Vomiting was noted at the onset in four cases and during the fever in one case. Five of the patients had diarrhea, which was more occasional than constant; five were constipated most of the time, and one showed no abnormality. They seemed both to enjoy and digest the generous dietary that was given. For a number of years the opinion has been gaining ground that typhoid fever patients were being fed on a too exclusively weak and liquid diet. While the latter was based on the idea that a bland, fluid diet was safest for an inflamed, irritated bowel, the loss of weight and extreme inanition that sometimes followed this plan had unfortunate results. Some patients cannot take sufficient milk or other fluid nourishment to repair the waste caused by the fever and keep up the general vitality. It must be remembered that all digestible food is in liquid form when it passes from the duodenum into the ileum, and that feces, consisting largely of dead bacteria, epithelial cells and the secretions of the bowel, usually become solid only in the lower part of the colon. It is difficult to see how such material can have any appreciable effect on ulcers usually located in the ileocecal region. A more generous and varied diet not only stimulates the jaded appetite and digestion, thus making the patient able and willing to take more nourishment, but the resisting powers are thereby increased and the dangers of relapses thus lessened.

Acting on this idea, the children were allowed the general ward diet with the exception of meat. This included milk, cocoa, eggs, bread, toast, crackers, cereals, jelly, potatoes, gravy, broths, custard, junket, apple sauce, orange juice, ice-cream and lady fingers. They received nourishment once every three hours throughout the day.

An effort was made to give them forty calories per kilo body-weight per day, but in not a single instance was it possible to make

them take the full required number of calories through the febrile stage. In some instances, sugar of milk or malt-sugar was added to the liquids in order to increase the total caloric value of the food but this also failed, since the children refused to take it. Dr. Dennett, who had this feature of the work in charge, concluded that while from a theoretical standpoint it would be beneficial to have them take the required number of calories, it was not practicable to carry out the caloric feeding in these cases, since children, unlike adults, cannot be forced to take food.

The success of this varied diet is shown in Table 2.

TABLE 2.—DATA CONCERNING TYPHOID PATIENTS ON LIBERAL DIET

Age Years	Weight			
	On Admis- sion Pounds	On Discharge Pounds	Gain Pounds	Loss Pounds
8	43 $\frac{1}{4}$	41 $\frac{1}{8}$	2 $\frac{1}{8}$
5	30 $\frac{5}{8}$	32 $\frac{3}{4}$	2 $\frac{1}{8}$	
3 $\frac{1}{2}$	31 $\frac{1}{8}$	33 $\frac{7}{8}$	2 $\frac{3}{4}$	
4	29	32 $\frac{5}{8}$	3 $\frac{5}{8}$	
2	24	23 $\frac{3}{4}$	$\frac{1}{4}$
3	22 $\frac{3}{8}$	30 $\frac{3}{8}$	8	
6	40 $\frac{9}{16}$	38 $\frac{3}{8}$	2 $\frac{3}{16}$
6	33	34 $\frac{1}{4}$	1 $\frac{1}{4}$	
4	22 $\frac{5}{8}$	30 $\frac{1}{4}$	7 $\frac{5}{8}$	
6	43 $\frac{1}{16}$	45 $\frac{1}{4}$	1 $\frac{5}{16}$	
5	37 $\frac{5}{8}$	37 $\frac{1}{4}$	$\frac{3}{8}$

It is seen that seven cases gained in weight during the fever, two showed a very slight loss and two an appreciable loss. The most remarkable cases occurred in a child of 3 years who showed a gain of 8 pounds after a fever lasting nineteen days, and another of 4 years gaining over 7 pounds after a fever of twenty days.

There were no very severe complications and no relapses. Under the former may be noted two cases of tonsillitis, two of otitis media, one hypostatic pneumonia, one pyelitis and one severe bronchitis.

Without a knowledge of the epidemic and the use of the Widal test, it is doubtful if most of these cases would have been properly diagnosed. In no case was the spleen palpable. They came in with the following diagnoses: Probable typhoid fever, 5 cases; Brill's disease, 1 case; meningitis, 1 case; miliary tuberculosis, 1 case; bronchitis, 1 case; no diagnosis, 2 cases.

I am indebted to Drs. Dennett and Steinmetz for aid in watching and collating the cases.

DIAGNOSIS OF WHOOPING-COUGH BY THE COMPLEMENT-DEVIATION TEST *

ALFRED FRIEDLANDER, M.D. AND E. A. WAGNER, M.D.
CINCINNATI

The recognition of such a scourge as whooping-cough, particularly when occurring in institutions in which children are segregated in large numbers, is a matter of great importance.

In his address on this subject before this Society last year, Morse emphasized the difficulty—and the value—of early diagnosis.

By the time the paroxysmal stage is reached, the infection, where children are gathered together, is widespread, and the resulting mortality high, as shown by carefully collated statistics.

The desire to find a definite method of early diagnosis led us to a study of the complement-deviation test. With our modified technic we have been able to make the diagnosis of pertussis in all stages of the disease, catarrhal, paroxysmal and convalescent. Particular emphasis is laid on the point that the diagnosis can be made early in the catarrhal stage, long before any whoop appears, and at a time when prompt isolation of the infected child will prevent the spread of the disease. Thus several children admitted to the open children's ward of the Cincinnati Hospital with a diagnosis of bronchitis, gave a positive early reaction, though there was neither vomiting nor whoop. They were immediately removed to the pertussis ward, and our open ward remained free of pertussis all winter. A preliminary report of our work has already been published¹ from which the following excerpt is taken.

When Bordet and Gengou² described the bacillus of whooping-cough in 1906 they used the complement-deviation test to control their bacteriological findings. From this time on, it has been known that the blood of patients in the late stages of pertussis, during convalescence and for some time thereafter, would give a positive test showing definite deviation of complement. More recently it has been shown that in the later stages of atypical cases of pertussis, it is possible to deter-

* Read at the meeting of the American Pediatric Society, Stockbridge, Mass., May, 1914.

1. Friedlander, A., and Wagner, E. A.: Jour. Am. Med. Assn., March 28, 1914, p. 1008.

2. Bordet and Gengou: Ann. de l'Inst. Pasteur, 1906, xx, 731.

mine the specific pertussis character of the infection by means of this test.³

Several observers have denied the possibility of making a diagnosis of pertussis even during the height of a typical attack or directly after convalescence by means of the complement-deviation test. Working in the Royal Serological Institute of Vienna, Bächer and Menschikoff⁴ report that in twenty-seven cases of pertussis, moderate and severe, in the height of the attack, and in convalescence, attempts were made to obtain positive complement-deviation reactions, without success in a single case. Only after vaccines, prepared from pure cultures of the Bordet-Gengou bacillus were given was the test ever positive.

Commenting on these and other similar findings, Bordet⁵ himself says: "I repeat that the power (of fixing the complement) is not seen early. In general it does not show itself markedly till toward the period of convalescence or cure." Netter and Weil⁶ have reached practically the same conclusion. In fact it would appear to be the consensus of opinion that the test has no diagnostic value in the early stages.

Our own results lead us to the opinion that the complement-deviation test is of the greatest possible value in the diagnosis at all stages. Our results are herewith presented in tabular form.

TABLE 1.—RESULTS OF COMPLEMENT-DEVIATION TESTS FOR WHOOPING-COUGH

	No.	Positive	Negative	Per Cent.
Cases whooping	18	18	0	100
Normals	16	0	16	100
Early cases catarrhal stage	12	11	1	91.6
Not whooping; course otherwise typical	1	1	0	100

These cases were taken both from our hospital service and from private practice, and all cases were carefully followed.

It will be noted that the 18 cases tested during the paroxysmal stage gave positive reactions: 3+ in each case. Nine of the cases were in the first week of the whoop, and 3 early in the second week.

3. Bordet and Gengou: *Centralbl. f. Bakteriöl., Abt. I, Orig.*, 1911, lviii, 537; Bordet and Brunard: *Bull. Acad. de méd. Belge*, 1910, xxiv, 320; Delcourt: *Presse méd. Belge*, 1912, lxiv, 19.

4. Bächer and Menschikoff: *Centralbl. f. Bakteriöl., Abt. I, Orig.*, 1912, lxi, 218.

5. Bordet: *Centralbl. f. Bakteriöl., Abt. I, Orig.*, 1912, lxvi, 276.

6. Netter and Weil: *Compt. rend. Soc. de biol.*, 1913, lxxiv, 236.

In no case did a normal give a positive reaction. This series included several cases of bronchitis. Of the 12 early cases, tested in the catarrhal stage, 11 gave positive reactions, and in each instance the definite whoop appeared later, thus confirming the serologic diagnosis clinically. The one case that gave a negative reaction was tested at the very beginning of the cough. The sister had given a positive test. Two weeks later the child with the negative test began to whoop.

TABLE 2.—TABLE OF ELEVEN POSITIVE REACTIONS TESTED IN THE CATARRHAL STAGE

No.	Duration of Cough Without Whoop	Time of Appearance of Whoop After Test
1	3 weeks	1 week
2	3 weeks	3 weeks
3	3 days	2 weeks
4	8 days	About 1 week
5	5 days	2 days
6	1 week	2 days
7	1 week	2 days
8	10 days	2 weeks
9	5 days	2 days
10	10 days	1 week
11	2 weeks	5 days

The one case giving a positive test that never whooped, occurred in a child with paroxysmal cough and vomiting lasting over a period of four weeks, evidently an atypical pertussis.

TECHNIC OF TEST

Our technic for the test has been as follows: A small amount of blood—about 15 to 20 drops—was taken from the patient's ear, finger or toe in small test-tubes or the Wright capillary tubes. For young children we have found the great toe very satisfactory.

The blood was kept at room temperature or placed in the incubator until coagulation had taken place. Serum was then separated more completely from the clot in the centrifuge. So far in our test we have used only fresh, active serum. Two drops of the serum were used in each test.

Hemolytic System: The Noguchi system was used because of its extreme delicacy and because of the small amounts of material—especially serum—required. In this system washed human corpuscles, 1 drop to 4 c.c. of salt water, are used.

Amboceptor: The amboceptor employed was prepared according to the Noguchi method, the serum being dried on filter paper. The complement was obtained in the usual way from guinea-pig—dilution 1 to 40. Aside from the delicacy of this hemolytic system, it is of great value in working with children because of the very small quantity of blood required. It is not necessary to take blood from the veins and the small quantity of blood required is easily obtained even from very young children.

Antigen: This is the most important factor in the test. The Bordet-Gengou bacillus was obtained in pure culture from the laboratories of Parke, Davis & Co. Most of our work was carried on with this culture. Cultures were

also obtained from the H. K. Mulford Co., and from Dr. F. B. Mallory of Boston. The latter culture came from a strain grown at Theobald Smith's laboratory.

Subcultures were made on Bordet's medium and an ascitic fluid agar. Lately we have used the ascitic fluid agar exclusively and our antigens were made up as follows: Seventy-two-hour growths were taken. The colonies, which were very tenacious, were scraped off the agar with a glass hook into sterile salt water. An emulsion was made and the bacteria again washed in salt water. It is important to do the second washing so as to rid the emulsion of any particles of agar. From this washed emulsion a standard suspension was made, and 0.1 to 0.2 c.c. of this used in the tests. Throughout the test, live bacteria were used. It will be noted that we have always used fresh, active serum and live bacteria, and we consider this innovation of great importance.

Controls: In each test known normal and known positive controls were used. In each series of tests the hemolytic system was tried out in the usual manner, using a water bath at 37 C. for incubation. After primary incubation for half an hour, the amount of amboceptor indicated by the preliminary test was added to our final test-tubes and the tubes again incubated in the water-bath.

In every instance independent readings were taken by each of us, always without previous knowledge of the clinical history of the given case.

The test is not at all difficult to carry out for any one with experience in serologic work. Using the precautions above noted, the readings have always been sharp, clear and unmistakable. It is not difficult to keep the bacillus growing on the ascitic fluid agar, which for the purposes of the test is a much more satisfactory medium than the original Bordet.

The point of particular importance is that by this method and by this test the diagnosis of pertussis can be made with absolute certainty in the catarrhal stage. Finally it is a matter of record that the success of vaccine therapy depends in large measure on the time of its application. The earlier the vaccine is given the better the results. If it be possible to diagnosticate whooping-cough in the catarrhal stage surely and definitely, its rapid cure seems assured. We have just recently begun therapeutic vaccine work. In two cases—father and son—occurring in the private practice of one of us, the test was positive in the catarrhal stage in both instances. Both patients whooped subsequently, confirming the diagnosis clinically. Both of these cases were treated with a vaccine prepared from one of our own subcultures. The father received five injections at four-day intervals, 600,000,000 bacteria being given at a dose. In three weeks his cough had ceased completely. The boy also received five injections of same dosage, and in three and a half weeks his cough was over.

We believe, therefore, that the test as outlined is worthy of full confidence and that it offers definite early diagnosis and thus points the way to a rapid cure of pertussis.

4 West Seventh St.—3104 Jefferson Avenue.

THE ARTIFICIAL COOLING OF SICK-ROOMS IN SUMMER

A PRELIMINARY REPORT *

HENRY HEIMAN, M.D.
NEW YORK

The mortality of gastro-enteritis in infants, despite all scientific efforts devoted to its amelioration, is so appalling, that each summer, in addition to employing what is best in the old methods of treatment, we attempt to devise newer and better ways of combating this formidable disease. It was with this in view that during my summer service of 1913, an endeavor was made to attack this malady in a way entirely different from any previously undertaken.

The etiology of gastro-enteritis has been and will be for years to come a much discussed subject. Without reiterating the well known conclusions of many pediatricists, based on theoretical considerations and practical observations, let us state that in our opinion also, gastro-enteritis is probably primarily a nutritional disorder, having as a secondary causal factor a bacteriologic basis. Both of these factors operate in winter as well as in summer. To account, then, for the marked prevalence of diarrheal diseases in summer we must consider a third potent cause, namely, the heat.

In order to determine the exact part heat really plays in the production of these summer diarrheas, and the effect of treatment in a routine manner with this important factor eliminated, a cooling plant was installed at the suggestion of Dr. Goldwater, superintendent of the hospital, in one small ward of the children's pavilion whereby the temperature of the room was kept constantly lower than that of the outside atmosphere. In brief, the method of cooling was as follows:

Outdoor air is forced by a motor-driven Sirocco fan through a water-chamber in which the water is cooled by brine coils. From this chamber the air is forced through an upper chamber filled with additional brine coils, thence through short ducts into the wards, where the cooled air enters near the floor level. Open transoms allow the warmer strata of vitiated air to

* Submitted for publication, May 27, 1914.

* From the Children's Service of Dr. Henry Koplik, Mt. Sinai Hospital, New York.

* Read at the meeting of the American Pediatric Society, Stockbridge, Mass., May 27, 1914.

escape from the top of the rooms. Some air also escapes through the entrance door when used by the nurse and the physician. The cooling plant proper is located in the basement under room No. 1, as shown on plan, Figure 1. It consists of a Greef air washer, a motor-driven blower and coils through which cold brine is forced, an eliminator for removing the free particles of moisture and heating coils for reheating the air, if so desired.¹

The temperature was recorded by means of two recording thermometers, one registering the outdoor temperature, the other that of the room. The relative humidity was ascertained by a sling psychrometer. Observations of the temperature and relative humidity were also taken in the general ward where no cooling was done.

Typical charts of the recording thermometers are reproduced in Figure 2, showing the records for the hours from 9 a. m., July 31,

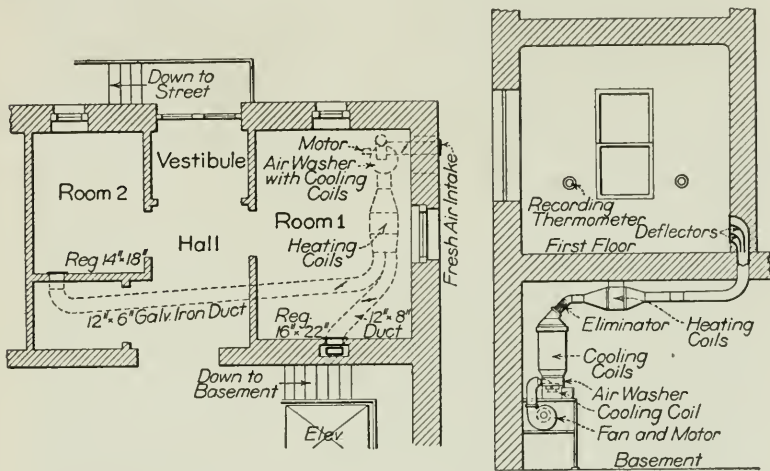


Fig. 1.—Location and details of air-cooling plant.

1913. The outdoor temperature, as will be noticed, was 86 F. at 9 a. m., rising gradually to an average of 92 between 1:30 and 4: p. m., then dropping gradually to 78 between 5 p. m. and 6:30 p. m., when it began to rise again. The indoor temperature of the room was maintained at an average of 72 between 9 a. m. and 3 p. m., rising gradually to 74 at 7 p. m., which latter temperature was maintained until midnight, then rising to 75 until 4 p. m., dropping again to 74 until 7 a. m. and 72 at 8:45 a. m. The temperature in the cooled room varied during the period of observation from 63 to 74. This latter temperature was reached only on one day when the temperature on the street rose to 93. The average temperature in the cold room for 252 readings was 69 during a period of forty-two days. The

1. From a description by A. M. Feldman, M. E., Consulting Engineer, in the Proceedings of the American Society of Heating and Ventilating Engineers.

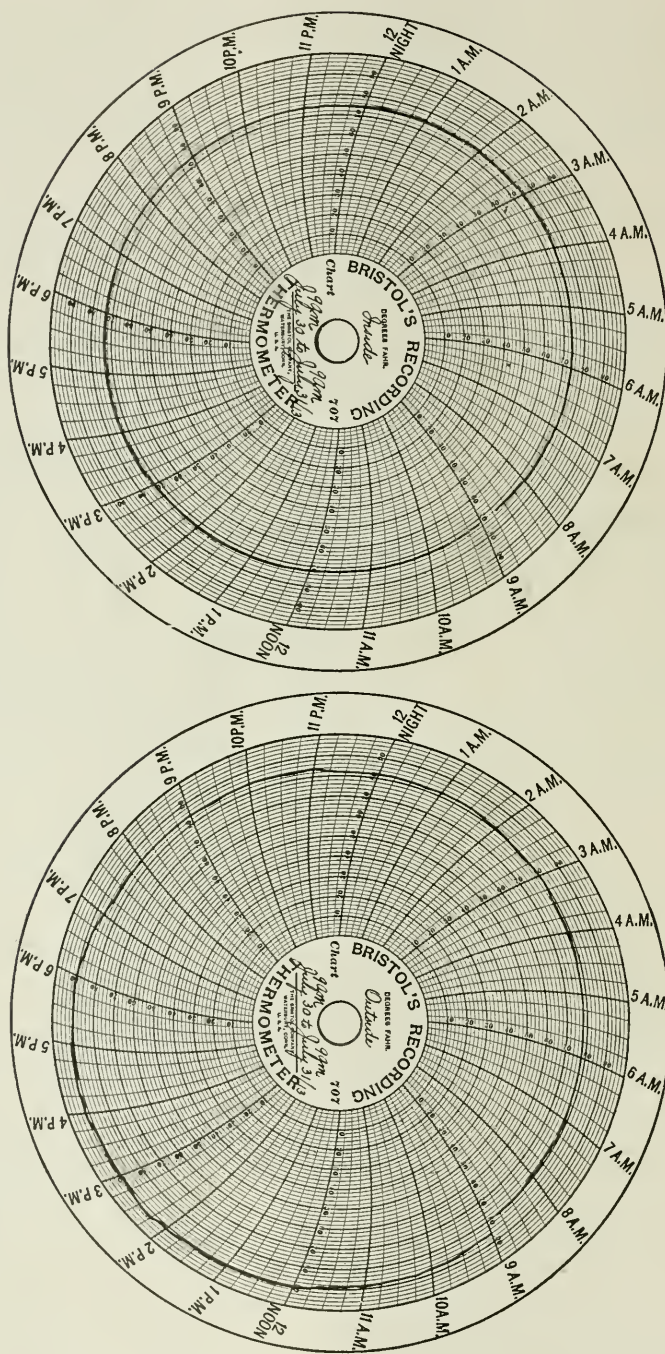


Fig. 2.—Charts showing record of inside and outside temperatures, July 30 and 31.

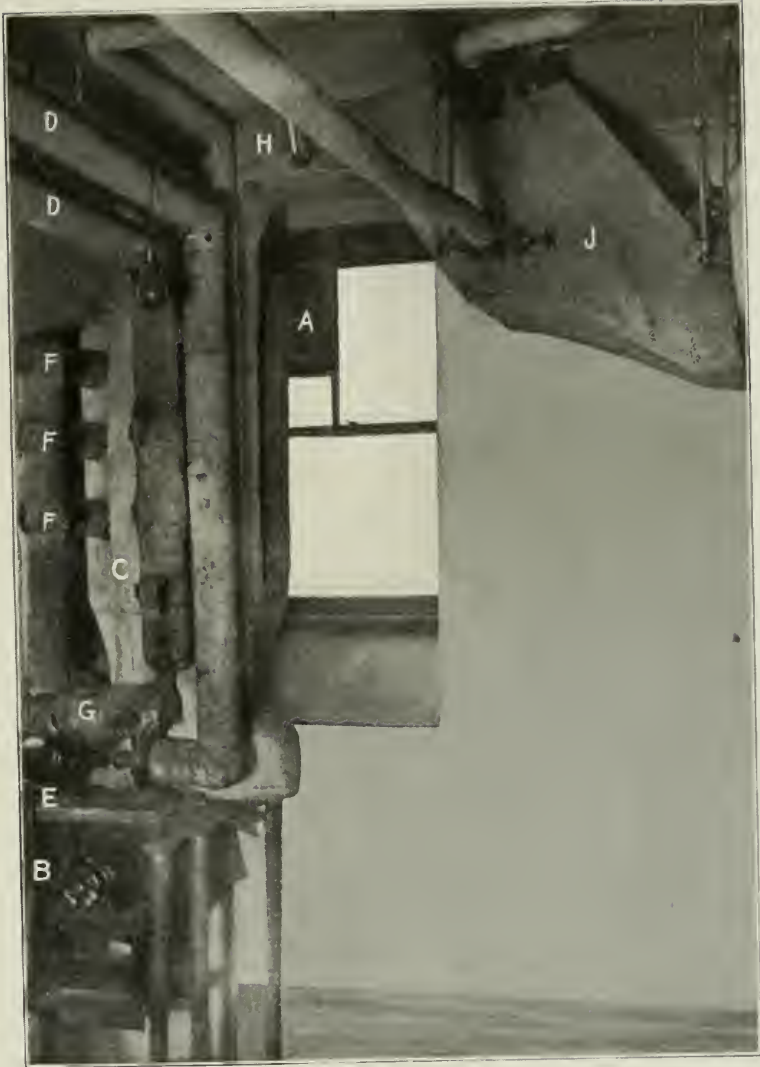


Fig. 3.—View of the air washing and cooling apparatus. The fresh air enters the duct at the point A in the upper sash of the window. At B may be seen the blower which delivers to the cooler-washer and cooling coils in chamber C. The pipes D D, are brine pipes tapping the return brine line of the general refrigerating system of the building. At E is the small pump for securing a positive circulation of the brine. The brine pump delivers to the washer through the pipe G and to the three coils above the washer F, F, F. At H is the delivery duct from the air washer and J is the reheating chamber, fitted, as indicated, with thermostatic control, the reheating coil also divided into three sections and the sections having hand valve control in the usual way. Incidentally the brine pipes are provided with thermometer wells and a thermometer is shown at the side of the duct to obtain readings of the air on delivery from the air-washer cooling system. A thermometer was also arranged for on the delivery side of the reheating chamber, so that arrangements are available for making a comprehensive test.

records of the outdoor temperature during the same forty-two days, taken at 8 a. m., 12 m., 4 p. m., 8 p. m., 12 p. m. and 4 a. m., were 77, 79, 79, 80, 74 and 70 F., respectively. The temperature of the cold room was at all times from 5 to 11 degrees below that of the outside air.

The relative humidity was observed at different intervals during the day. In the artificially cooled room, the relative humidity varied between 41 and 76, making an average of 60 for readings taken on twenty-five different days. In the main ward, the relative humidity varied during the same period from 35 to 80, with an average of 59.

It is interesting to note that while low temperatures were obtained in the cold room, the relative humidity was approximately the same percentage as that in the main ward with higher temperature, thus indicating that the absolute humidity was reduced by the process of cooling.

Thirteen selected cases were treated, the average period of treatment being about two weeks. By selected cases is meant patients suffering from gastro-enteritis, ruling out premature and moribund infants. Six of the thirteen were in poor condition at the time of admission. One of these died shortly after entering the hospital. All the others were discharged from the hospital well. The treatment in all these cases was not different from that ordinarily carried out; this included *Eiweissmilch*, skimmed milk or barley water, plus the usual symptomatic medication.

Inasmuch as only thirteen cases of gastro-intestinal diseases were treated in the artificially cooled ward, it is hardly justifiable to present definite conclusions as to the therapeutic value of this measure. Gastro-enteritis was not particularly prevalent during the summer of 1913, and the number of cases treated in the hospital was very much below the number usually treated; in fact, the thirteen patients who were treated in the cooled ward were practically all the gastro-enteritis cases available for our first tentative studies. Thus there was no opportunity for comparison of the behavior of these cases with that of patients treated for the same disease in the open wards, under ordinary conditions. While unable at the present time to draw far-reaching conclusions, we have nevertheless gained the impression that the babies treated in this ward were, on the whole, more comfortable, cried less often, looked less sick and less parched, rested and slept better than the patients kept in the other wards of the children's service during the same time.

It is not our intention to belittle the present methods of treatment of this disease, as well as the efforts of the Board of Health, the Social Welfare Department, milk depots and other associations for

the prevention of infant mortality, but simply to introduce this additional therapeutic measure as a valuable adjuvant in the eradication of this malady. The only cases in which this method may be harmful are in weaklings, premature and moribund infants, in whose cases extreme heat is a powerful factor in sustaining life. In all other cases of gastro-enteritis, no matter how severe, the artificial cooling of the sick-room will in our opinion prove to be an extremely helpful measure.

I hope to have the opportunity of studying this important question further this summer. I wish to thank Dr. Louis H. Levy and Dr. A. Brody for their kind assistance in carrying out these observations.

30 West Eighty-Eighth Street.

CIRCUMCISION IN THE MASTURBATION OF FEMALE INFANTS*

ROWLAND G. FREEMAN, M.D.
NEW YORK

The masturbation of female infants while really not common occurs with moderate frequency. At the meeting of this society in 1907, Dr. B. K. Ratchford in his presidential address reported fifty-two cases of masturbation in infancy observed by members of this society, only four of which occurred in male infants.

This habit, if neglected, leads to a considerable amount of moral depravity, and on the other hand, it may be fairly controlled by proper treatment. It is, therefore, a serious condition which is fairly controllable and one to which too little attention has been devoted. I say nothing of the masturbation of male infants, for sufficient attention is paid to the hygiene of the male sexual organs so that the sort of irritation which leads to masturbation in infants rarely exists in boy babies. On the other hand, in the female infant there exist fairly regularly marked adhesions between the sensitive clitoris and the surrounding tissues so that on examination the clitoris is frequently found to be buried in these adhesions.

In a normal child these adhesions seem to cause little irritation; but in the nervous, sensitive child they may cause intense irritation and lead to the formation of a habit which, if untreated, may become permanent and exert a most injurious influence over the future development of the child.

The treatment of this condition is both general and local. The general health should be improved by such hygienic measures as are available, and all sources of nervous irritation and excitement should be, as far as possible, removed; but no cure can ordinarily be accomplished by such measures alone. The common use of an apparatus for separating the thighs is of little avail, and the only curative treatment is that applied to the removal of the active source of irritation, the adhesions of the clitoris. These may be separated without the use of an anesthetic. The operation is very painful, and such separation under these conditions is difficult and apt to be followed by the formation of other adhesions. The only satisfactory method of treat-

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* Read at the twenty-sixth annual meeting of the American Pediatric Society, at Stockbridge, Mass., May 26, 1914.

ing this condition is by circumcision, an operation which should be performed by one who is accustomed to do it, the foreskin being removed as completely as possible.

The result of this operation is most satisfactory. In many cases no recurrence of the habit is noticed after the operation, while in others recurrences will occur; but they are found to be due to adhesions which have formed notwithstanding the circumcision.

The existence of so serious a complication in a young infant long before the development of the sexual activity leads one to wonder whether more attention should not be paid to the condition about the clitoris in all young girls with symptoms of nervous irritability. It has been said that the clitoris is an electric button which rings up the whole nervous system. It is my belief that more attention should be paid to the hygiene of this region.

The histories which one obtains of these cases are not always clear. The common history of a child putting its fingers on the genitals at every opportunity, while showing evidence of some irritation, is naturally not sufficient for a diagnosis of masturbation. The real condition is often misunderstood by the parents, but when masturbation exists, a clear history of an orgasm can be obtained after close observation on the part of the attendants.

A few illustrative cases of this sort I will enumerate.

CASE 1.—A female infant aged 10 months was noticed frequently to rub her thighs actively for a certain period and then to become quiet, breaking into a perspiration. This habit had been noticed for several weeks and was becoming more frequent. Examination showed the clitoris to be entirely buried in adhesions. These were somewhat broken down and the clitoris moderately cleared without, however, any effect on the habit, so that an operation was advised. A complete circumcision was done two months ago and at the same time a large adenoid was removed. Since that time no masturbation has been noticed although carefully watched for.

CASE 2.—A girl aged 3 years had probably from the history been masturbating for more than a year, this habit having become worse, especially at bedtime and in the morning. The real character of this habit had only just become evident. The child was circumcised under chloroform anesthesia and at the same time a large adenoid was removed. More than two years have elapsed since this operation without any recurrence of the habit, although a year after the operation the child had an attack of chorea which lasted for about a month.

CASE 3.—A child aged 5 years had weighed only 5 pounds at birth, but had done well until she was 8 months old, when she contracted a colitis followed by the condition known as the infantilism of Herter, from which, however, she recovered again in the course of a year. She is a frail, nervous child, and it has only recently been noticed that she masturbated. A partial separation of the adhesions without an anesthetic did not remove the habit, so a circumcision was performed under anesthesia, and she has never been known to masturbate since, although five months have elapsed since the operation.

Other cases have shown less favorable results from the operation.

CASE 4.—A child aged 5 years, frail and nervous, with red hair but usually well, was found to masturbate. A circumcision was done under anesthesia fol-

lowed for a time by a cessation of habit; but three months later the habit was again noticed and on examination new adhesions were found to have formed, and the breaking down of these was followed again by a cessation of the habit for six months. Since that time there have been several periods when the habit was resumed, always associated with adhesions about the clitoris. These, however, have become less frequent and now there is no history of a recurrence during the past year, five years after the operation.

CASE 5.—A child aged 18 months with a cerebral palsy and poor intellectual development gave a history of straining which was supposed to be associated with constipation. She was a premature child weighing 3 pounds at birth who had convulsions on the fourth day. She did not talk or stand, and both the right leg and right arm were weak and of little use. She was said to strain when lying down, would get red in the face, perspire, burrow her head in a pillow and then go to sleep. The clitoris was found to be buried in adhesions and a circumcision was performed. Two months after the operation there were still some slight attempts at masturbation and three months later there were almost none. Five months later it was reported that she had been free from attacks, but for a week past these had recurred, and on examination it was found that new adhesions had formed. She was much better after these were broken down. Six months after the operation she was brought to New York on account of her renewal of the habit, and the clitoris was found fairly buried in adhesions. These were broken down without an anesthetic. This child left four years ago for Australia and it has been impossible since then to keep in close touch with her condition, although the father writes me that she has entirely ceased straining. Here was a difficult case on account not only of the recurrence of the adhesions but also of her mental deficiency.

CASE 6.—Another case very resistant to treatment but always benefited by the breaking down of adhesions was a child I first saw ten years ago who was then 10 months old. She was frail, nervous and had red hair. When only 10 days old what was apparently a typical masturbation was noticed. She was treated with braces, which seemed to control the habit temporarily. She had a suspicious eruption during the first year but never any clear evidence of syphilis. She had a typical orgasm in my office, covering her face with her skirts and rubbing her thighs together, taking a number of deep inspirations and then breaking into a sweat. The clitoris was found bound down by adhesions and a circumcision was performed, after which she was better. Seven months after the operation the mother reported that there had been an entire cessation of the habit until two weeks before. The clitoris was found again buried in adhesions, and a second circumcision was performed under an anesthetic. Since that time there has been a steady gradual improvement in her condition. Occasionally new adhesions have been broken down, but without an anesthetic, and periods of months have elapsed with no attempt at masturbation and there has been no history of the habit now for three years.

CONCLUSION

The masturbation of female infants occurs in nervous children, the stimulating cause being adhesions about the clitoris such as exist in practically all female infants.

The treatment of this condition by braces alone is palliative and not curative. The only curative treatment is by separation of the adhesions and circumcision, and the result of such operative interference is often satisfactory.

211 West Fifty-Seventh Street.

MIDDLE EAR COMPLICATIONS OF MEASLES IN IMMIGRANT CHILDREN *

H. C. CODY, M.D.

Assistant Surgeon, U. S. Public Health Service

ELLIS ISLAND, N. Y.

The occurrence of middle ear suppuration as a complication of measles has been recognized, but the extreme prevalence of this complication has not been realized. In fact, so far as I know, there never have been any real data produced in any of the works by authorities on the contagious disease, as to the incidence of middle ear disease in measles.

The following, taken from the records and statistics of the Contagious Disease Hospital at Ellis Island, will give some idea of the extent and nature of the disease as met with in immigrant children, and may indicate to some extent its occurrence in all cases. Of course the conditions met with in Ellis Island differ greatly from ordinary cases in general practice, not only in the class of patients, but in the stage of disease and in the care the patients have had previously on board ship; and undoubtedly the percentage of all complications is higher than ordinary.

First of all, I would like to do away with the idea as held by some people, that the form of measles found in foreign children differs from that found in the native born. True measles is the same irrespective of country or nationality.

Middle ear suppuration is by all means the most common complication met with in all cases. In infants less than 18 months old it ranks second only to bronchopneumonia, and the reason of this may lie in the conditions of life on board ship.

From the time the hospital was opened in June, 1911, until Dec. 1, 1913, there were admitted in all 1,769 cases of measles. The average age of all patients was 4.81 years; and of these 321 cases, or 18.2 per cent., developed middle ear disease.

In addition to these, several cases proved to be diphtheria carriers, and these developed middle ear disease, which showed Klebs-Loeffler bacilli in the discharge and proved extremely obstinate.

The length of time an uncomplicated case of measles remained in the hospital varied from seven to thirty days, accounted for by the

* Submitted for publication, April 3, 1914.

degree of disease on admission. The average time of all cases was approximately two weeks. Those cases developing ear trouble (exclusive of mastoid involvement) remained on an average for 45.12 days.

Bacteriologic examination of the discharge from the ears gave a preponderance of *Staphylococcus aureus*. In some a bacillus (probably Hoffman's) was found. In those cases in which a streptococcus appeared, the child was much sicker and more resistant to treatment. This last holds also of the diphtheria infections, as shown by the records of two children who developed mastoids with a stay in the hospital of 213 and 241 days, respectively. Even then they were not entirely well.

It is interesting to note the comparatively low incidence of mastoid involvement. Out of the whole 321 cases, only twenty-nine, or 1.6 per cent., developed this troublesome feature, with an average stay in the hospital of 75.64 days.

The onset of middle ear suppuration occurred most frequently after the measles rash had disappeared, and usually several days after admission. In a few cases it was present on admission. In nearly all cases it appeared suddenly and with little or no pain. In very few cases did we see acute otitis and paracentesis of the drum was a rare event. Moreover, little pain was experienced during the progress of the disease. Usually, but by no means always, was there an elevation of temperature for twenty-four to thirty-six hours before the suppuration occurred. In general the process began and persisted as subacute.

The treatment found most effective consisted in keeping the middle ear clean. This was accomplished by frequent and copious irrigations at low pressure. The solution found to be most beneficial was 1 to 10,000 mercuric chlorid made up in normal salt solution. About a pint was used of this for each ear three or four times daily with the fountain syringe at a height of about two feet above the ear. After each irrigation the canal was wiped dry with sterile cotton.

The most obstinate period of the treatment was at the last when there was very little discharge. This would often resist treatment for days, and as we made it a rule not to discharge a patient until the ear had been dry for two days, the length of stay in the hospital was often materially increased. Very often the convalescence was hastened by instilling drops of alcohol and mercuric chlorid after each irrigation.

The ultimate results of course cannot be determined, as it is impossible to follow up these children; but in the majority of cases the hearing of the children on leaving the hospital was good; the drum membrane more or less completely restored.

To sum up then, suppurative otitis media occurs as a complication of measles in immigrant children; that is to say, in children subject to

unfavorable hygienic surroundings both at home and on board ship, in nearly 20 per cent. of cases. Mastoid involvement is not common, and the disease yields to treatment comparatively readily. The disease is essentially subacute (rather than chronic) and the apparent results as affects hearing are good.

A CASE OF TUBERCULOUS MENINGITIS COMPLICATED BY INFLUENZAL MENINGITIS *

H. K. FABER, M.D.
NEW YORK

Tuberculous meningitis complicated by purulent meningitis is a rare event. In a search through the literature I have been able to find records of twenty-one cases only. Paisseau and Tixier¹ reviewed the subject in 1909 and collected nine cases, adding one of their own. They, however, overlooked six cases reported, respectively, by Heiman,² Lenhartz,³ Heubner⁴ (three cases) and Kneass and Sailer.⁵ Since 1909 two more cases have been reported by Guinon and Grenet,⁶ and Dupérié.⁷ To these should be added three cases from the records of the Babies' Hospital and the one here presented in detail.

The organism found in these instances of mixed infection were the meningococcus, the pneumococcus, the streptococcus, *M. tetragenus*, the colon bacillus and an unclassified Gram-negative diplococcus growing freely on all media. In no case was *B. influenzae* found. Nine of the twenty-one cases were due to the meningococcus.

The fact that influenzal meningitis associated with tuberculous meningitis has not hitherto been described is a somewhat surprising fact, for influenza has long been known as a particularly frequent and severe complication of tuberculosis. Pfeiffer in his report⁸ of the successful cultivation of the influenza bacillus called attention to the fact that the mortality of patients with pulmonary tuberculosis was very high during the influenza pandemics of 1891 and 1892. From the sputum of such patients he was able in a number of instances to

* Submitted for publication, May 13, 1914.

1. Paisseau, G., and Tixier, L.: Méningite et surinfection. *Gaz. d. hôp.*, 1909, lxxxii, 979.

2. Heiman, Henry: Tubercular Meningitis. *Arch. Pediat.*, 1897, xiv, No. 2.

3. Lenhartz: Weitere Erfahrungen über die Lumbalpunktion. *Deutsch. med. Wchnschr., Vereins Beilage*, 1897, p. 130.

4. Heubner: Ueber den Meningococcus. *Deutsch. med. Wchnschr. Vereins Beilage*, 1897, p. 109.

5. Kneass and Sailer: A Case of Tuberculous Meningitis with Secondary Infection. *Jour. Nerv. and Ment. Dis.*, 1904, xxxi, 660.

6. Guinon, L., and Grenet, H.: Méningite à méningococques et à bacilles de Koch associés. *Rev. internat. de tuberc.*, 1912, xxi, 33.

7. Dupérié, R.: Gommès tuberculeuses hypodermiques multiples chez un nourrisson. Méningite terminale à méningococques et à bacilles de Koch. *Arch. de méd. des Enf.*, 1912, xv, 599.

8. Pfeiffer, R.: Die Aetiologie der Influenza. *Ztschr. f. Hyg.*, 1893, xiii.

isolate the influenza bacillus. Petruschky,⁹ in a study of the secondary infections of pulmonary tuberculosis, found that next to streptococcus infection influenza was the most common complication. Similar conclusions, based on cultures from the sputum and from the lungs at autopsy, were reached by Kirchensteiner,¹⁰ Schabad,¹¹ Klieneberger,¹² Kruse¹³ and Wohlwill.¹⁴ Wohlwill, in a very careful study of tuberculous lungs at autopsy, found that by making cultures from the finer bronchi he could isolate *B. influenzae* from sixteen of the seventy-three cases he examined, or from 22 per cent. Even more striking are the results obtained at the Babies' Hospital during the last three years. Cultures from the lungs have been made in fifty-four cases of pulmonary and general miliary tuberculosis and in these the influenza bacillus was found twenty-three times, or in 42.5 per cent.

In view of these facts it is perhaps surprising that no case like the present one should have been reported before.

AUTHOR'S CASE

The patient whose history is the subject of this report was admitted to the Babies' Hospital, Feb. 3, 1914, for convulsions. He was an Italian child, 5 months old. For the previous two months the mother had had a cough and this was the only suggestion of exposure to tuberculosis that could be obtained. Two weeks before admission, for a reason not given, the baby was weaned and since then had not thrived, though no other untoward symptoms had been noticed. Three days before admission the patient had a general convulsion lasting several minutes, after which the head became retracted and remained so ever since. Between the onset and the time of admission to the hospital he had about twenty more convulsions, and in the intervals was restless and irritable and slept little. He did not vomit.

On admission there was seen an irritable, poorly nourished child who looked acutely ill. The head was retracted and the neck was very stiff. The fontanelle, though slightly bulging, was not tense. The only abnormal signs in the chest were a few coarse râles at the angle of the right scapula. The liver and spleen were felt just below the costal margin. The legs were semi-flexed and slightly spastic and the knee-jerks exaggerated, but Kernig's sign was not present.

Examination of the blood showed 19,000 leukocytes, of which 35 per cent. were polymorphonuclear and 65 per cent. were lymphocytes. Lumbar puncture (February 4) showed 15 c.c. of clear fluid under normal pressure. In this there were 145 cells per c.mm., 92 per cent. of which were lymphocytes. No microorganisms were found in the smear.

9. Petruschky: Zur Behandlung fiebernder Phthisikern, Charité Ann., 1892-3, xvii and xviii.

10. Kirschensteiner: Studien zur Bacteriologie der Lungen und Bronchialeiterungen, Deutsch. Arch. f. klin. Med., lxxv.

11. Schabad: Die Mischinfection bei Lungentuberculose, Ztschr. f. klin. Med., 1897, xxxiii.

12. Klieneberger: Ueber hämoglobino-phile Bazillen bei Lungenkrankheiten, Deutsch. Arch. f. klin. Med., 1906, lxxxvii.

13. Kruse: Zur Aetiologie und Diagnose der Influenza, Deutsch. med. Wchnschr., 1894.

14. Wohlwill: Ueber Influenzabazillen im Bronchialbaum, Münch. med. Wchnschr., 1908, lv, No. 7.

The Von Pirquet skin test was strongly positive.

A second lumbar puncture was done the next day and showed a fluid having the same general characteristics as the first. A smear from it showed, however, a number of short, slender, Gram-negative bacilli which were morphologically identical with *B. influenzae*. An attempt to grow these on blood-agar failed.

A blood-culture taken at this time showed a profuse growth of two organisms, *Staphylococcus albus* and *B. influenzae*. The former was regarded as a contamination from the skin; the significance of the latter was not apparent.

February 6 a choroidal tubercle was discovered in the right fundus and on February 14 tubercle bacilli were found in the spinal fluid. The fluid though still perfectly clear was now under increased pressure, contained 375 cells, practically all lymphocytes, to the c.mm. and formed a film after standing twelve hours.

These findings established the diagnosis of tuberculous meningitis and inclined us to regard the presence of other organisms in the blood and spinal fluid as accidental. The only evidence from the spinal fluid of a cerebrospinal infection other than tuberculosis was the presence of influenza-like organisms in a single smear and this was not corroborated by culture.

THE BABIES' HOSPITAL

Name S. S.

Age 5 mos.

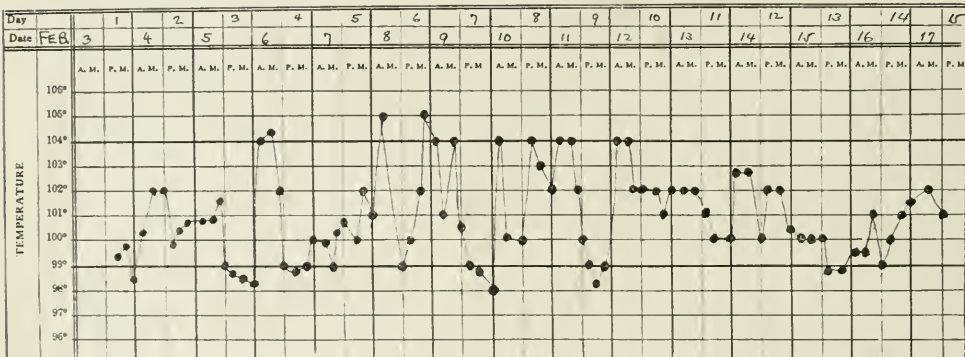


Chart showing long-continued, intermittent type of temperature in author's case.

Nevertheless, the clinical symptoms were very different from those of uncomplicated tuberculous meningitis. From the time of admission to that of death the patient had almost continual general clonic convulsions. The attitude was most striking. The head was retracted, the back was curved in extreme extension, the legs were flexed on the thighs and the thighs were flexed on the trunk. The muscles were all spastic. Frequent facial twitchings were observed and there was nystagmus. In view of the autopsy findings it is worth noting that no unilateral motor symptoms were ever noted.

The temperature, in marked contrast to that usually seen in tuberculous meningitis, ran a high and irregular course. So many similar temperatures at this season had been found in this hospital to be due to influenza that a culture was taken from the bronchial secretion and in this *B. influenzae* was demonstrated.

About ten days after admission signs of partial consolidation were found in the left upper lobe. Whether this was due to tuberculosis or to an intercurrent broncho-pneumonia was not clear.

The patient died from exhaustion sixteen days after admission.

The autopsy showed glandular, pulmonary and general miliary tuberculosis. The oldest lesions were in the left bronchial lymph-nodes, which were matted together round the main bronchus and in the hilum of the lung. In the left upper lobe were a number of caseous areas and a walnut-sized cavity just under the pleura. Surrounding this cavity was a zone of broncho-pneumonia.

The brain showed two distinct processes. The pia everywhere was studded with small miliary tubercles and there was at the base a fibrino-purulent exudate such as is usually seen in tuberculous meningitis. There was also present over the convexity of the left hemisphere an abundant, thick grayish-yellow, purulent exudate. This was not present on the right side.

The left middle ear was normal but the right contained a small quantity of thick pus.

Smears and cultures from the pus on the left convexity showed *B. influenzae* only, while a smear from the right ear showed both influenza bacilli and pneumococci. A culture from the bronchopneumonic area in the left upper lobe also showed a pure growth of *B. influenzae*. The strain recovered from the brain was injected into a rabbit and a guinea-pig and proved fatal for both within twenty-four hours.

Analysis of the clinical symptoms and the laboratory findings in this case reveals two striking points of difference from the picture usually seen in tuberculous meningitis; namely, the evidence of extreme cortical irritation and the long-continued, intermittent type of temperature (see chart). It was thought that the temperature might be explained by the respiratory influenzal infection, but the signs of cortical irritation, though frequently commented on during life, were adequately explained only by the autopsy. Considering the comparatively low leukocyte count and the lymphocytosis and the character of the cerebrospinal fluid, it was impossible to make a diagnosis of purulent meningitis during life.

The portal of entry for the influenzal infection in this case was evidently the respiratory tract, whence we may assume that it entered the blood-stream and then lodged in the meninges.

Why the cerebrospinal fluid failed to give any evidence of supuration is difficult to explain. Several hypotheses occur to one, but perhaps none is necessary. In a case of meningitis reported by Dr. Josephine Hemenway¹⁵ nothing abnormal was found in the spinal fluid before death, yet at autopsy there was discovered over both frontal lobes a purulent exudate from which the pneumococcus was grown in pure culture. This case demonstrated beyond a doubt that the products of meningeal inflammation do not of necessity migrate into the cerebrospinal fluid.

In conclusion, I wish to thank Dr. L. Emmett Holt for permission to publish this case, and Dr. Martha Wollstein for assistance in the pathological work.

Babies' Hospital.

15. Hemenway: Two Cases of Acute Meningitis of the Convexity. Arch. Pediat., March, 1908.

PROGRESS IN PEDIATRICS

ACTIVE IMMUNIZATION AGAINST DIPHTHERIA BY MEANS OF VON BEHRING'S VACCINE, AND THE DIPHTHERIA TOXIN SKIN REACTION *

BORDEN S. VEEDER, M.D.
ST. LOUIS, MO.

I. ACTIVE IMMUNIZATION

The weak point in the immunizing use of diphtheria antitoxin lies in the short duration of the passive immunity thus conferred. The injected antitoxin is rapidly broken down and eliminated until in the average case there is not sufficient antitoxin left at the end of ten days to afford further protection. (Von Behring, Park.) While this ten day period may be enough to protect the average individual who has been in contact with a case of diphtheria, it is not adapted to protect those who are constantly or repeatedly exposed to infection, as for example nurses or physicians on service in a diphtheria ward, or patients in the wards of a children's hospital. The rapid destruction and elimination of antitoxin is due in large part to the use of a serum obtained from an animal of a foreign species. Park found that if a guinea-pig received 10 units of diphtheria antitoxin obtained from a horse (heterologous serum) there was only $\frac{1}{2}$ unit left at the end of seven days and $\frac{1}{20}$ of a unit at the end of fourteen. When, on the other hand, a guinea-pig was given 10 units of guinea-pig antitoxin (homologous serum) there was 1 unit left at the end of fourteen days. Matthes gave a 4 kg. child 350 units of an homologous serum. Following the injection the content of the blood serum in antitoxin reached a height of $\frac{1}{5}$ units per c.c., and one month later $\frac{1}{20}$ of a unit per c.c. could be demonstrated.

In practically every non-fatal case of diphtheria there is an active production of antitoxin as a result of the reaction of the body to the absorbed diphtheria toxin, which persists for a varying length of time. Park mentions a case of diphtheria in which the blood showed 60 units of antitoxin per c.c. at the end of the fifth day, 90 per cent. of which was produced by the patient. The average case forms very much less than this. In this connection the findings of Kissling are most interesting. Kissling studied the production of antitoxin in physicians and nurses working in diphtheria wards. Those who had never had clinical diphtheria but who had been working about the wards for a long time

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showed high amounts of antitoxin in their blood serum, while those recently assigned to duty showed low amounts and frequently contracted the disease. In other words an insensible active immunization had gradually taken place in those who had been on duty in the diphtheria wards for some length of time. The recent work of Schick and his coworkers would seem to show that active immunization is an exceedingly common occurrence, and that a large percentage of individuals—although they may never have had clinical diphtheria—possess sufficient antitoxin to protect themselves against infection except probably during severe epidemics.

The idea of the production of active immunization for purposes of prophylaxis is by no means new, and has been suggested by a number of workers in this field in past years. In 1909 Theobald Smith reported that he had obtained an active immunization in guinea-pigs, which lasted over several years, by the injection of toxin-antitoxin mixtures. Mixtures containing a slight excess of toxin produced the best immunity. Smith at this time suggested the use of toxin-antitoxin mixtures in man, and recognized the limitations of such a method. He found that diphtheria toxin alone produced a very slight degree of immunity with severe local lesions. Later, together with Brown, he reported the production of immunity in guinea-pigs by the injection of toxin in amounts so small that local necrosis did not occur. The immunity obtained in this way was sufficient to enable the guinea-pig to withstand one-half the lethal dose without a local reaction.

The first attempt to produce active immunization in man by means of toxin-antitoxin mixtures was reported at the 1913 meeting of the Kongress für Innere Medizin at Wiesbaden by Hahn, who presented the results of the use of such a vaccine prepared by von Behring at Marburg, and during the past year a number of papers on this subject have been published by von Behring and his associates. While the idea of active immunization by toxin-antitoxin mixtures is not new, as we have shown, von Behring claims originality through the results of his studies with such mixtures. It is not within the scope of this review to enter into a discussion of the relationship and combination of toxin and antitoxin, and we simply state von Behring's claim of the reversibility of such combinations. He found that a mixture in which 1 unit of toxin was neutralized by 1 unit of antitoxin for the guinea-pig, was not necessarily atoxic for other species of animals. Thus if 1 unit of toxin is combined with 20 to 40 units of antitoxin and the mixture injected into a monkey, the toxin causes death, and it is necessary to use 80 to 100 guinea-pig antitoxin units to neutralize 1 unit of toxin for the monkey.

The so-called "von Behring's vaccine" consists of a mixture of strong diphtheria toxin and antitoxin in such proportions that the toxin

is just neutralized, or is in very slight excess, when tested on a guinea-pig. A number of different mixtures have been used which are designated as M 1/M 11, MM 1, etc., and which vary somewhat in their proportions. The mixtures remain active for ten weeks after preparation. At first the vaccine was injected subcutaneously and the formation of antitoxin in the blood serum studied by Römer's method. It was found that from twenty to twenty-five days elapsed before the development of immunity.¹ It was later found that if the injections were given intracutaneously a stronger immunity resulted and the interval between the injection and the development of immunity was reduced to ten days. This largely overcomes the most serious practical objections to the use of the vaccine.

The vaccine produces a reaction at the site of injection which is similar to the local tuberculin reaction. By testing the blood of vaccinated individuals it has been found that the degree of the local reaction corresponds to the amount of antitoxin formed, and hence furnishes a simple and reliable index of the degree of immunization produced. It is impossible to test the blood for its antitoxin content where a number of people are vaccinated, and Hahn and Summer have put this phenomenon to practical use by recording the degree of immunization according to the degree of the local reaction, and have elaborated a scheme for recording the local reaction according to the area and degree of reddening, infiltration, and scaling that occurs. According to Kleinschmidt and Viereck the local action of the toxin of the vaccine does not depend on the antitoxin in the blood, as is the case when diphtheria toxin alone is injected intracutaneously. A negative reaction with the latter is evidence of antitoxin in the blood, and it has frequently been observed that individuals with antitoxin in the blood are more susceptible to the vaccine than those without. Antitoxin in the blood—which depends on an active immunization from previous infection and which is found in some 50 per cent. of people—apparently leads to a hypersensitiveness toward the toxic agent. Kratz has shown that a toxin-antitoxin mixture which is toxic for an actively immunized animal is neutral for a control animal of the same species. It is suggested that a previous active immunization leads to a more rapid cleavage of the toxin-antitoxin mixture.

Hahn in his original report gave the results of the use of the vaccine in forty cases. No bad results were noted. The formation of antitoxin was studied in all of these cases which are largely

1. The antitoxin content of the blood serum which affords immunity apparently lies between 1/10 and 1/30 units per c.c., except perhaps in case of infection with organisms of high virulence.

of theoretical interest. Matthes likewise studied the formation of antitoxin. The results in one case (K) were as follows:

December 23, K. was given 0.25 c.c. of MM 1/4 subcutaneously. Previous to vaccine injection the blood showed an antitoxin content of $\frac{1}{8}$ units per c.c. Later tests were as follows:

10 days after injection—160 units of antitoxin per c.c.
16 days after injection—175 units of antitoxin per c.c.
21 days after injection—20 units of antitoxin per c.c.
12 weeks after injection—8 units of antitoxin per c.c.

(v. Behring reckons that it will be two years before antitoxin falls to 1/100 units per c.c., in this case.)

Zangmeister reported that new-born children do not react to large doses of the vaccine. Kleinschmidt and Viereck studied the antitoxin formation in twenty-seven children and came to the conclusion noted above, that intracutaneous injections are more active and that the degree and rapidity of immunization corresponds to the strength of the local reaction.

Following these rather theoretical studies, in which no bad results were observed, Kissling, and Hahn and Summer, used the vaccine in a large number of cases in order to test its practical value. Kissling injected 310 patients in the wards of his hospital at Hamburg who had been exposed to diphtheria. Of these 111 received two injections and no cases of diphtheria developed after vaccination. One hundred and ninety-nine were injected once and eight of these subsequently developed clinical diphtheria. The cases which developed were in the scarlet fever and pertussis wards.

Scarlet fever: 197 patients were immunized; 108 injected twice; 89 injected once; 5 cases developed.

Of these 1 developed on the fourth day after injection; 1 on fifth day after injection; 1 on nineteenth day after injection; 1 on thirty-fifth day after injection; 1 on thirty-seventh day after injection. The last three were very mild.

Pertussis: Thirty cases immunized; three cases of diphtheria developed.

Kissling observed four severe reactions when the vaccine was injected into the arm and prefers to inject into the skin of the back along the line of the scapula.

Hahn and Summer tried out the vaccine in certain villages and small cities where diphtheria was epidemic. They found a tremendous difference in the susceptibility of different individuals to the vaccine, some reacting less than others to doses fifty times greater. For this reason they first inject a small dose (0.01 c.c. intracutaneously) and if a severe reaction is obtained a second injection is not given, as the first was found to give satisfactory immunity. If a mild reaction is obtained, a second injection with a doubled dose is given on the third day, and if no reaction followed the first injection a 10-times dose is given at the second injection. They advise two or even three

injections a day apart unless the first or second reactions are very severe. Children were vaccinated in five villages and cities and as many did not return for examination after the first or second injections, the cases are divided as follows:

1. Complete immunization: good repeated reaction.
2. Doubtful immunization: slight reaction after first and did not return after second injection.
3. Unsatisfactory immunization: did not return for examination after first injection.

An example of their results is as follows:

CITY OF EGELN (5,300 INHABITANTS)

Cases from January 12 to November 11.....	=72	} 7.5 per cent. mortality.
First immunization, November 11.....		
Cases November 11 to December 18.....	=27	
	Total No. Children	Cases of Diphtheria which Developed after November 11
Non-immunized	1,089	21
Inside first ten days.....		4
Unsatisfactory immunization	89	0
Doubtful	130	1
Complete	304	1

Thus 20 per cent. of the non-immunized developed diphtheria and 10 per cent. of the immunized. If the four cases developing in the first ten days are omitted, the percentage of immunized cases is only 3.3. Of these four cases, one was so mild that antitoxin was not used. The totals were as follows:

	Total No. Children	Cases of Diphtheria
Complete immunization	633	2
Doubtful immunization	255	2
Unsatisfactory immunization	209	1
Cases developing in first ten days after injection.....		10
Cases developing among non-immunized.....		51

Of the two cases developing among the "completely immunized," one was abortive and the other was a clinical case without bacteriological control.

A "negative phase" between the time of the injection and the development of immunity has not been noticed by any who have used the vaccine so far. On the contrary Hahn and Summer note that the ten cases of their series which developed within ten days after injection were all characterized by a mild abortive course. The antitoxin portion of the vaccine has not produced an hypersensitiveness to further injections of antitoxin used for curative purposes in those patients who developed diphtheria subsequent to the injection of the toxin-antitoxin mixture.

The vaccine is still in an experimental stage and its final value and usefulness remain to be determined. So far no bad or unpleasant results have been reported. If further use supports these early impressions the vaccine will probably find a definite place in the

prophylactic treatment of diphtheria, as numerous indications for the use of such a means occur at once to the clinician.

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II. THE DIPHTHERIA TOXIN SKIN REACTION

NATURE OF THE REACTION

In 1909 Schick found that if a solution of diphtheria toxin was applied to the skin in the same manner that tuberculin is used in the von Pirquet tuberculin test, it produced a reaction in many persons very similar to the tuberculin reaction. Later, by using the intracutaneous method, he was able to regulate the amount of toxin absorbed and this has led to a number of studies which are of both theoretical and practical importance.

The toxin used by Schick and his associates is a dilution of such strength that 0.1 c.c. equals 1/50 of the lethal dose for a 250 gm., guinea-pig. The lethal dose of the toxin which Schick uses is 0.005, and hence he injects 0.1 c.c. of a 1-1,000 dilution. In those who react an area of reddening and infiltration develops within twenty-four hours, reaching its maximum in forty-eight hours, and which heals with scaling and a characteristic central pigmentation. Although the reaction is similar to the local tuberculin reaction, its interpretation is directly opposite. The diphtheria toxin is a direct toxic agent and by control tests of the blood serum it has been found that *a negative reaction is always associated with the presence of diphtheria antitoxin in the blood* of the person tested. While

as a rule a positive skin reaction is an indication of the absence of antibodies, some persons react positively for some unexplained reason who possess a greater amount of antitoxin in the blood than 0.03 units per cubic centimeter.

It has been found that if a negative reaction follows the injection of a 0.1 c.c. of a 1-1,000 dilution of toxin, the individual tested has at least 0.031 units of antitoxin per c.c. in his blood when tested by Römer's method. A person with a higher concentration of antitoxin will react negatively to a smaller dilution of antitoxin and vice versa. Thus the outcome and the degree of reaction are dependent on two factors—the strength of the toxin used and the presence of antitoxin in the blood.

The specificity of the diphtheria toxin skin reaction is shown by its suppression or inhibition by the simultaneous injection of antitoxin in individuals who have previously given a positive reaction. In this connection the work of Schick and Maygar, who studied the simultaneous injection of diphtheria toxin and tuberculin, is interesting. Previous studies of tuberculin and toxin reactions in the same individual by Rolly, Entz and others, led them to conclude that the reaction to tuberculin was a general reaction toward toxic substances. Schick and Maygar tested 315 individuals with both tuberculin and diphtheria toxin at the same time and only obtained the same reaction (both positive or both negative) in 163 cases. In 153, or almost 50 per cent., the reactions were different.

THE REACTION AS A PRELIMINARY TEST FOR PROPHYLACTIC INJECTIONS OF ANTITOXIN

As noted above, it has been found that if a negative reaction follows the injection of 0.1 c.c. of a 1-1,000 dilution of toxin, the blood serum contains at least 0.031 units of antitoxin per cubic centimeter. This is sufficient to afford immunity against infection with the diphtheria bacillus under ordinary circumstances.

A large number of tests on normal individuals have been made and the reactions obtained are given in the following tabulation. Many of these have been controlled by Römer's method.

	Total	Positive	Negative	Per Cent. Negative
New-born infants.....	291	10	275	93
First year of life.....	42	18	24	57
2 to 5 years.....	150	95	55	37
5 to 15 years.....	264	131	133	50

It is thus seen that a large percentage of individuals are immune to diphtheria. The age period giving the lowest percentage of negative reaction (2 to 5 years) is the same as that in which the highest incidence of clinical diphtheria is found. As far as could be deter-

mined the reaction remains the same for a period of at least four weeks.

The practical value and application of such results is obvious. Whenever it is necessary to immunize against diphtheria for prophylactic purposes, a diphtheria toxin skin test will show in twenty-four hours those who already possess immunity. Only those reacting positively to the toxin require passive immunization with antitoxin. As roughly 50 per cent. possess immunity this will reduce the number of prophylactic injections one-half. The real extent of such a reduction is seen when one considers that, according to Park, two injections for immunization are given in New York City to one for curative purposes. The liability to sensitization to horse serum is coincidentally lessened to the same extent.

AS A TEST FOR ANTITOXIN CONTENT OF THE BLOOD

In the past the manner of measuring the quantity of diphtheria antitoxin in the blood has been indirect. The blood serum of the individual tested has been added in different dilutions to a definite quantity of toxin and injected into guinea-pigs. The blood content in antitoxin is calculated from the dilution which just neutralizes the toxin.

Schick and Michiels having once found that 0.1 c.c. of a 1-1,000 dilution of their toxin requires 0.031 units per cubic centimeter of toxin in the blood to suppress the toxin reaction, have been able to test directly the quantity of antitoxin by varying the strength of the dilution. If a negative reaction follows a 1-1,000 dilution, a 1-500, 1-200, etc., dilution was used until a strength was reached at which a positive reaction occurred. It is necessary first to find the strength of a toxin on guinea-pigs, after which it may be used directly in different dilutions.

USE IN ANTITOXIN EXPERIMENTS

Until the elaboration of the toxin skin reactions, all experimental work in regard to the relations of toxin to antitoxin have been carried out on animals, and our ideas regarding the administration and efficacy of antitoxin in man have very largely been based on animal experimentation. Schick and his associates have carried out a large number of experiments on children in regard to these questions.

Children who reacted positively to a toxin skin test were given antitoxin in different amounts and at the same time a toxin reaction was made. Fairly large quantities of antitoxin were needed to suppress the reaction (2,000 units intramuscularly). In another series of experiments toxin tests were made at two and three hour and

longer intervals and the effect of large doses of antitoxin noted. Practically no effect could be made on toxin injected more than three hours before the administration of antitoxin. Reactions from injections of toxin made forty-eight, seventy-two and ninety-six hours after the administration of fairly large quantities of antitoxin were suppressed.

Schick comes to the conclusion that the action of antitoxin is chiefly immunizing, and that injections should be made as early as possible and either intravenously or intramuscularly. The value of antitoxin in severe cases depends on whether a lethal dose of toxin has been absorbed before the antitoxin was administered.

OTHER USES

A few attempts have been made to produce active immunity by repeated injections of small amounts of toxin. Three injections of 0.1 c.c. of a 1-500 dilution were made two weeks apart. As no weakening of the reaction was observed at the third injection the result was looked on as unsuccessful. No indications of hypersensitiveness were observed.

As there is no antitoxin present free in the blood in acute diphtheria, the use of the reaction for diagnostic purposes has been suggested. Thus in a suspected case or questionable diagnosis a negative reaction—indicating the presence of antitoxin—would speak against the diagnosis of diphtheria.

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1806 Locust Street.

DIGESTIVE DISTURBANCES OF ARTIFICIALLY FED BABIES *

TRANSLATED BY

IRVING M. SNOW, M.D.
BUFFALO

During the last twenty years there has been much change in the interpretation of symptoms occurring in the digestive diseases of babies. The older physicians regarded acute and chronic gastrointestinal disorders as being always due to diseases of the stomach and intestines. Fermentation dyspepsia, fermentation catarrh, gastroenteritis, cholera infantum, dysentery, ileocolitis. These were compared with similar conditions in adults, allowance being made for the slighter resistance in babies which favored a severe course of the disease.

Widerhofer made a classification on anatomic grounds, dividing the various symptom-complexes into:

1. Purely functional.
2. Catarrhal.
3. Ulcerative-inflammatory lesions of the intestines.

These were clinically distinguished by the character of the stools and by the constitutional symptoms; thus, he speaks of acute and chronic dyspepsia, enterocolitis and enteritis with inflammatory lesions in the large intestine. A fourth form was the murderous cholera infantum.

This description is most valuable. Yet there were many intermediate and transitional forms and but few clear-cut typical cases.

Although severe inflammatory infections of the intestine do exist, yet they are less frequent in importance and frequency than purely functional disorders. It is also true that persistent functional disturbance may cause anatomic changes.

In all varieties of cases a uniform and normal condition of the intestines may exist where the old teaching would suggest severe organic lesions. With some digestive disorders the symptoms and course are more dependent on general visceral changes than intestinal inflammation.

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* This article is a condensed translation of Finkelstein and Meyers' treatise on diseases of the digestive tract in Feer's new book on Diseases of Children.

Thus, bacterial infection does not play the important rôle formerly supposed. Many symptoms are due more to alimentary food-intoxication than to bacterial toxins. The vomiting, fever, diarrhea are usually due to disturbed metabolism; hence the term introduced by Czerny "Disturbance of Nutrition."

Formerly great importance was ascribed the bacteria and bacterial products in polluted milk, yet this factor is of really slight importance compared with improper dosage or character of food. The maintenance of health and development is intimately associated with good functional energy and normal tolerance. A child with good tolerance may be injured by under-nourishment or over-nourishment; with correct feeding a baby may become ill through primary weakness of digestion, a misproportion between the demands of appetite and the process of assimilation.

Inanition also plays a serious rôle in infantile pathology. The food may be too highly diluted or lack important food element, as in gruels and proprietary foods. There are also disturbances due to over-nourishment; the digestive functions are overworked and weakened. The tolerance has been exceeded even if the quantity and character of the food recipe be theoretically correct. Overfeeding may cause sickness in a feeble baby. The diet may not exceed the physiologic need, yet it may make great demands on an especial function, leading to its exhaustion.

A breast-fed baby with careless handling thrives better than a bottle baby with the most correct regimen.

GENERAL PATHOGENESIS

Most children are easily fed. A few show uncertain digestion and have a stormy infancy. Overfeeding leads to delayed assimilation, food-stagnation and bacterial decomposition. Sickness from relative underfeeding is seen in weakly children of the neuropathic exudative diathesis. With artificially-fed babies tolerance is easily exhausted, and cow's milk mixture with the exact chemical formula of human milk has a radically different effect and often injuriously affects a baby. The difficult digestion of casein is a myth, shown by the analysis of stools, but there is no doubt of the occasional injuries by fats and sugars. This reaction is not primary, but is secondary to fermentation of the whey. The whey of human milk, on the contrary, acts as a stimulant to digestion. The fat and albumen of cow's milk in whey will cause sickness, while if the same fat and albumen be mixed in human whey, the child will thrive.

The poor digestion of fats and sugars is due to pathologic fermentative processes, resulting in acid formation causing a local reaction on the intestinal mucosa, increased peristalsis and secretion of mucus. The child's health deteriorates and the protective processes of metabolism are lessened and poisonous substances formed.

Bacterial poison causes cell injury of the internal organs as well as of the intestinal tube.

Excessive atmospheric heat hinders heat evaporation and injures the working capacity of the cells; symptoms like sunstroke often appear, coma and hyperpyrexia, which latter is relieved by hydrotherapy. Artificially fed children do not resist heat well.

Contaminated milk was formerly held to be the most important and frequent cause of diarrheal disease, but intestinal fermentation is usually endogenous and will develop in a sterile food from primary digestive incapacity; the present theory is that within certain limits heat has a damaging effect on the child, reducing digestive tolerance so that food injuries easily occur. A bottle baby with disturbed nutrition has less heat resistance than a child which is nursed.

GENERAL SYMPTOMATOLOGY

More variety exists than was formerly supposed. The symptoms affect not only assimilation and tissue-building, but also internal metabolism and heat production and regulation, therefore the description should not be limited to vomiting and diarrhea. We observe albuminuria, cerebrospinal irritation, anomalies of heart and lungs, which often may be relieved by a change in diet.

All of us admire the fine color and beautiful contour of a healthy baby. It has normal stools and by the continual formation of antibodies effectively resists infections, which, if they do occur, run a benign course. It also has a breadth of tolerance for food, thriving on all sorts of mixtures and passes easily through the extreme heat of summer.

A baby with disturbed digestion shows emaciation, increased or diminished muscular tonicity, pallor, excitability or apathy, fluctuations in temperature and suffers a lowering of resistance against bacterial influence. Alimentary fever is often confused with infection; it may be distinguished by its course and its disappearance by a change in food.

Children with disturbed nutrition show a lessened tolerance for food. A healthy child with an increase in diet will react by a gain in weight. A sick child will show a paradoxical reaction. An increase of food aggravates its symptoms and causes a loss in weight.

Example.—Three children (1) healthy; (2) slightly disturbed; (3) severely disturbed. Thirty grams cane sugar added to twenty-

four-hour quantity of food for two or three days. Healthy child increased in weight. Second child slightly ill with mild fever, diarrhea and a stationary weight. Third child has a temperature of 100.5 F., violent diarrhea and lost several hundred grams.

This reaction to food is the measure of the reduced functional power. The more the patient is disturbed by small increases of food, the more serious is its condition. Such children are very sensitive to infections, heat, etc.

CLASSIFICATION: NUTRITIONAL DISTURBANCES

- Disturbances: Alimentation; various foods; injuries.
Czerny: Disturbances: Infection; polluted milk.
Disturbances: Congenital weakness of constitution.

Finkelstein:	{ Mild forms without destructive processes	{ (1) balance disturbance (2) dyspepsia
	{ Severe destructive processes	{ (3) decomposition (4) intoxication

Also, disturbances from inanition—feeding on gruels, proprietary foods; treatment by repeated periods of starvation.

Infection, heat, etc.

Whole question is of lessening of digestive tolerance.

Balance disturbance—lessened tolerance for fat in milk.

Symptoms: Insufficient gain in weight; firm stools.

Dyspepsia	{ Lowering of tolerance for fat of milk	{ Symptoms: Insufficient gain in weight; vomiting; diarrhea; sometimes constipation.
	{ Lowered tolerance for carbohydrates	{ Vomiting; diarrhea; colic; paradoxical reaction for food.

Decomposition Marasmus Atrophy	{ Severe damage for digestion of fats and carbohydrates	{ Abrupt loss in weight; subnormal temperature.
		{ Slow pulse; paradoxical reaction; strong reaction to heat and infection.

Intoxication	{ A condition developing on the basis of dyspepsia and marasmus if large quantity of food containing whey and sugar is given.	{ Fever; cerebral disturbance; albuminuria; glycosuria, deep breathing, vomiting and diarrhea.

BALANCE DISTURBANCE — CZERNY — SLIGHT MILK INJURY

Retarded development without marked symptoms of illness. The weight curve rises slowly, fluctuates and remains stationary or diminishes. The patient appears smaller than the normal child; has a poor color, flabby muscles, distended abdomen, irritable disposition; the stools are dry and gray (soap stools); it occasionally vomits; is easily infected.

- Two types exist. 1. Fed chiefly milk.
2. Milk and carbohydrates.

The child may always show poor progress on milk mixture or the food may contain too much milk and too little carbohydrate.

The baby may do well for a while or may have a congenitally weak tolerance, or one reduced by an infectious illness.

Pathogenesis.—Cream is usually the injurious food element, and there is often rapid improvement on a diet poor in fat and rich in carbohydrate, which improvement is arrested by adding fat again. It is probable that the low digestive power for fats is secondary to weakening of intestinal function, through abnormal fermentation of sugar of milk; a rapid cure may often be effected by substituting another carbohydrate, dextri-maltose or a cereal gruel.

Sometimes an injured tolerance for carbohydrates causes the condition to advance to dyspepsia.

There is a change in metabolism, chiefly in fat absorption, the alkaline secretions of the intestine are increased and combined with fatty acids; there is increased secretion of mucus; the stools are of a whitish color; the bilirubin is changed to urobilin. To produce a soap stool the large intestine must be strongly alkaline—soap stools are not pathologic and may be observed with normal development.

Diagnosis.—If a baby with sufficient nourishment, 100 calories per kilo of weight per day, with no diarrhea or vomiting makes no progress, one may make a diagnosis of disturbed balance. The condition may be confused in children reduced in weight by illness, for convalescents have a greater need of nourishment, often taking 120 to 140 calories per kilo per day. One must also consider mild cases of decomposition in whom a change in food has stopped a diarrhea. These cases show a paradoxical reaction, dropping in weight if food is increased.

Lastly, there are anomalies of growth from unknown constitutional causes which defy the most skillful feeding.

Prognosis.—With appropriate dietetics the prognosis is very good. The number and quantity of meals should be regulated, the milk reduced and the carbohydrates increased. The type due to excess of milk is most easily treated by adding a little cereal gruel, a malt food or two carbohydrates in proportion of 2 to 5 per cent. of the total recipe. If one carbohydrate fails, try another; not more than five meals daily; quantity of food should be watched until the tolerance is known. Malt soup is often effective in obstinate cases.

Recipe for Malt Soup.—50.0 wheat flour, $\frac{1}{3}$ liter milk, malt extract 100.0, $\frac{2}{3}$ liter water. Mixed, cooked, strained.

Or buttermilk, clean and not too acid, mixed, with a flour-gruel and cane-sugar are excellent for younger babies.

Dextrimaltose may be considered constipating. From 2 to 3 per cent. of carbohydrates should be given. With proper dietetics, increased weight and good stools should soon occur. If malt-soup or buttermilk is given, after six or eight weeks an effort should be made to place the baby on a normal diet. A cure is established only when a suitable milk mixture agrees with the baby.

If the baby's condition still remains unsatisfactory in spite of carbohydrates, the outlook is less favorable; low carbohydrate toleration leads to fermentation. If all means of artificial feeding fail, breast milk is advised as in the treatment of dyspepsia.

DYSPEPSIA

Dyspepsia may be primary or a result of primary balance disturbance. The digestive capacity of the stomach is insufficient for the food given. There results pathologic fermentation, producing increased peristalsis and diarrhea — the chief symptoms of dyspepsia. The baby suffers from poor appetite, vomiting, slight motor insufficiency of the stomach, the free HCl is diminished, the volatile fatty acids increased, the abdomen is distended and there is colic. The stools are increased in number, are thin, contain mucus; the odor is foul and sometimes sour. The color of the stools is green; the bilirubin is oxydized to biliverdin. As a result there occurs the following: Fat soap stools; small white or yellow lumps, on warming, producing fat crystals; gruel (flour) stools are pasty and foamy; blue with iodine; red with erythrodermin. As to the question of undigested casein stool, little yellow lumps formerly supposed to be casein, are really fatty acids and bacteria.

Only after feeding raw milk will stiff cylinders of casein appear in the stools.

Formerly dyspepsia was divided into fat and starch (*Mehl*) dyspepsia. This classification is not justified for the appearance of undigested food elements in the stool does not prove that this element is the cause of the trouble. Thus, fat diarrhea does not come from primary insufficiency for fats, but from carbohydrate fermentation, causing increased peristalsis and fat in the stools. By withdrawing carbohydrates the fats can again be utilized.

Pathogenesis.—The local symptoms of dyspepsia are due to the increased production of fermentative acids from pathologic decomposition of carbohydrates, sugar and starch. Again, it may be emphasized that casein, so far from injuring the intestines, is most effective in combating an acid fermentation and exercises a curative influence.

The carbohydrates used in feeding have important differences as to fermentation. The sugar of milk ferments most easily; cane sugar

less so; dextrimaltose is slow to ferment, hence the apparent constipation following its use.

The tolerance of an intestine for carbohydrate as well as fats depends much on the fluid in which they are dissolved or suspended. The same quantity of sugar in undiluted whey will more quickly cause dyspepsia than the same amount in water or in diluted whey. As a cause of dyspepsia in bottle babies, whey, even if regarded as free from sugar, plays an important rôle.

We have an acute dyspepsia and chronic dyspepsia, a temporary or persistent lowering of digestive function.

Diagnosis.—The chief thing in diagnosis is to separate dyspepsia from mild enteral and paraenteral infections which may also cause an irritation of the intestines. It must be remembered that infections are often associated with disturbed nutrition. An infection is present when temperature and mucous stools continue in spite of reduction in carbohydrates.

The physician is cautioned not to regard intestinal irritation from an infection as being due to fermentation, and institute a long, unnecessary course of underfeeding.

A dyspepsia being diagnosed, the physician must consider whether he is dealing with a previously healthy child or with a marasmus patient. This is most important as to treatment and prognosis. The history should be reviewed; the first attack of diarrhea is probably dyspeptic; recurring diarrhea and loss of weight indicate that the digestive strength of the child has suffered, and point to marasmus.

Prognosis.—In a previously healthy child the prognosis is good; recurring attacks in very young babies, or in emaciated patients are most serious.

DIETETIC TREATMENT

The safest treatment in all forms of dyspepsia is human milk; it is most necessary to babies in the first weeks of life where artificial feeding is so dangerous. The dose of woman's milk should be generous, although at first caution is advisable.

In acute dyspepsia, in a fairly healthy patient where the cause of attack is a misproportion between the child's appetite and his digestive power, there should be a short period of fasting, with copious draughts of saccharin tea for six or twelve hours; only exceptionally for a longer period. Complete emptying of stomach and intestine is effected by lavage and irrigation, and laxatives. One-third of the usual amount of food, well diluted, should be given. The nourishment should be rapidly increased so that the period of underfeeding may be as short as possible.

As to the kind of food, the offending food elements, fats and carbohydrates, should be avoided; also the injurious effects of whey should be remembered. A thin gruel, mixed with skim milk, is advised, and later dextrimaltose may be added. No sugar of milk. Skim-milk and buttermilk are usually well digested.

This dietetic treatment causes a sudden fall in weight, later a stationary condition, normal temperature and fewer stools.

After a few days the child's tolerance for carbohydrates should be tested.

Many patients, however, do not respond to this treatment, and the diarrhea continues. These children either have an infection or are on the verge of marasmus. To continually underfeed these children is to kill them.

Finkelstein recommends the use of albumen milk for these cases.

Children with chronic dyspepsia do badly under continued underfeeding. There is no acute depression, but a chronic weakness of tolerance and the continual trauma of hunger is injurious. The best carbohydrate is 2 to 3 per cent. dextrimaltose. If no improvement in the stools occurs, use human milk or albumen milk.

DECOMPOSITION — ATROPHY — MARASMUS

The chief symptom is the loss in weight which sinks slowly, at times very suddenly. The baby is emaciated, has a senile appearance, the abdomen is distended, the complexion gray.

At first the child is excitable, crying and taking food greedily; later it is languid, apathetic. The inclination is very noticeable to slow, irregular heart action and subnormal temperature, which may be later associated with edema and cyanosis.

The urine contains no albumen or sugar. The stools are dyspeptic and frequent; sometimes fluid, sometimes solid. The firm stool indicates an arrest of the process. Often the feces contain a large amount of fat. Occasionally the feces are dark red or black from hemorrhage from a peptic duodenal ulcer.

Such patients are most sensitive, showing an immediate severe reaction to unsuitable food, infections, etc. A cold, bronchitis or hot weather may cause high fever and collapse; purulent infections of the skin, pyelitis and pneumonia indicate the diminished immunity of the child.

Decomposition in very young babies, if not quickly improved by diet, is soon fatal. With older children there are periods of remission and improvement. A not unusual ending is a fatal hemorrhage from a duodenal ulcer. Some children die with symptoms of alimentary intoxication. Death may be quite sudden, especially after a therapeutic

hunger period. A hopeful case may succumb quickly to an intercurrent infection.

Pathology, Metabolism.—It was formerly supposed that marasmus was an inanition due to destruction of the digestive glands from chronic inflammation, but the intestine of an atrophic child may show normal anatomic relations. Decomposition is probably due to extreme functional depression as shown by the paradoxical reaction in feeding. The more nourishment the baby swallows the more rapidly it emaciates. A sudden drop of a pound or two is due to loss of water and salt. The melting of tissues goes on more slowly.

The prognosis depends wholly on the dietetic treatment. If errors are avoided and the case is not seen too late, very bad cases may be cured; if one-third of the original weight is lost, the condition is hopeless.

Diagnosis.—We must distinguish marasmus from the symptomatic emaciation of tuberculosis and other cachexias and also from inanition. Mild forms of decomposition may be confused with balance disturbance or dyspepsia. The history of recurring diarrhea or rapid loss in weight is important. The final test is the behavior of the digestion in feeding. With a fairly strong food mixture a marasmus child will show fever, diarrhea and a drop in weight.

Treatment.—The cure of the decomposition is possible if the fermentation which causes the deterioration in digestion is removed and the tissues are supplied with water and salts. Often the physician commences treatment as he does in dyspepsia, with a hunger period and small and increasing doses of food, but a marasmus child cannot endure starvation and should, if possible, be nursed. The danger of hunger is exhaustively considered under "Inanition." If insufficient food is given, the digestive strength is ruined.

With human milk the subtle curative agent is in the whey, which is somewhat offset by the difficult digestion of fat and sugar. If one gives too much the baby is upset; if too little, it grows rapidly worse. Finkelstein gives the breast milk in a bottle, 200 to 300 grams daily in eight to ten feedings, with copious draughts of saccharin tea, without a hunger period, to avoid the fatigue of nursing. The milk is continually increased so that after a week the baby is taking from 100 to 130 or 150 calories per kilo of weight daily.

At first the child may grow paler and thinner, but not after the second week. Then follows a period when the general condition improves, but there is no gain in weight. No change in the wet-nurse should be made. We are dealing with a period of repair. Cells are constructed slowly with human milk, which is poor in albumen and salts.

In a month the improvement may be hastened by one meal daily of malt soup or of buttermilk, with a small amount of dextrimaltose.

A complete restoration to health will not occur earlier than two or three months; then ordinary food mixtures may be tried. It must be remembered that the child may have an idiosyncrasy against cow's milk.

If no human milk is available, mixtures of skim-milk or buttermilk diluted with a thin gruel may be used; often an increase in strength of the food will occasion a serious diarrhea. Finkelstein strongly recommends albumen milk in such cases.

The idea of albumen milk is to limit the dangerous acid fermentation by lessening the percentage of sugar of milk in the whey.

3.0 Albumen sweetened with saccharin. Maltose should be added in the proportion of not less than 3 per cent.

2.5 Fat; 450 calories per liter.

0.5 Sugar.

A great advantage of albumen milk is that sufficient food may be quickly given without danger of fermentation. The risk of underfeeding and inanition is thus avoided. The amount of albumen milk may be quickly increased to 180 or 200 gm. per kilo daily. Total daily quantity should not exceed a liter. After a day or two the stools are firm and fewer in number. The weight curve ceases to sink, becomes stationary and then increases.

With advanced marasmus, to evacuate the intestines quickly a six- to twelve-hour hunger period with tea may be advisable, followed by 200 to 300 grams a day of albumin milk in ten doses; the amount is quickly increased and the number of bottles diminished. If the fall in the weight curve is not arrested in eight days, dextrimaltose should be increased.

If this technic is followed, the number of failures is surprisingly small.

Lack of success is due to:

1. Too slow an increase, producing inanition.
2. Too late and insufficient carbohydrate.
3. Omitting carbohydrates if the stools do not improve.
4. Reducing or withdrawing carbohydrate if a recurrence of diarrhea, fever or of emaciation occur.

In only extreme conditions should these changes be made and only for a short time.

Feeding with albumen milk should continue in young babies ten weeks; older babies six to eight weeks. After this, ordinary food mixture may be digested. A cure may be considered complete when after a course of albumin milk, followed by a milk mixture, the child continues to thrive.

INTOXICATION

An alimentary intoxication is a general toxic condition in a child with disturbed digestion who is given food exceeding its digestive power. The lower its functional tolerance is, the smaller the amount of food is which will produce the intoxication.

Symptoms.—The first symptom is fever, whose alimentary nature is proven by the fact that the temperature quickly becomes normal if nourishment is withheld. With the mildest type there is a slight rise in temperature; with a severe attack the fever may be 104, 105, 106 F.

The alimentary fever may be the only symptom or may be associated with diarrhea; usually the patient loses weight, is languid and shows signs of kidney irritation. These early symptoms are immediately, or after one, two or three days, followed by extreme depression, diarrhea, nervous symptoms, deep breathing, albumin and casts in the urine, and a serious drop in weight. At first the nervous condition is one of languor and somnolence. The child, if aroused, sinks immediately back into its lethargy. The face twitches, the eyes are sunken. In the worst cases the patient lies in a coma, or has general convulsions, transitory paralysis. Usually there is high fever, but a bad case of marasmus may show no feverish reaction.

The respiration is of a toxic type—deep, rapid, like a hunted animal. The stools are frequent; at first contain food debris, later are watery, greenish-yellow; are mixed with mucus. They become strongly alkaline from the abundant alkaline intestinal secretion.

Vomiting is often a serious symptom, recalling the clinical picture of the old-fashioned cholera infantum. The weight may sink from 500 to 1,000 grams in a few days. The skin is dry, shrunken, features drawn, fontanelles sunken; the muscles may be contracted and cramped.

The rapid loss of fluids quickly leads to collapse. The pulse is small, the heart weak, the extremities cold and cyanosed; the urine contains sugar from an alimentary glycosuria.

There may be a leukocytosis, reaching 30,000.

The great variety of symptoms show how many organs are involved. We may separate several different symptom-complexes—a comatose cholera form and cerebral type.

Pathologic anatomy.—The morbid changes are not extensive and do not correspond with the serious illness. In the stomach and intestines there is a serous or serohemorrhagic catarrh. Peyer's patches are swollen and hyperemic. Microscopically the wall of the gut shows a round cell infiltration.

Etiology.—The great similarity of an infantile alimentary intoxication to true cholera and cholera nostras of adults caused the older

physician to speak of cholera infantum and to ascribe the malady to an infectious origin, accusing contaminated milk. While such symptoms may occur in the course of parenteral and other infectious diseases, yet no pathogenic specific germ has been found to explain the symptom-complex. On the contrary, the most careful clinical observation shows that the condition is a food intoxication from exceeding the subject's digestive tolerance, and the origin of the disease is due to a decomposition of food. The use of polluted milk is therefore not essential, since the intoxication may originate from aseptic food.

The fact that food is the cause of the malady is proven by the effect of withdrawing food and giving water freely.

In all cases not complicated by an infection, the temperature at once falls; if food be taken again the fever returns. The fever-producing agents are the carbohydrates combined with whey constituents. If these substances are given in large quantities the fever is complicated by a toxemia. Large amounts of fat have also a toxic effect. This fat intoxication is, however, not primary, but is due to a sugar injury, which has severely damaged the function of metabolism.

Nature or Toxic Condition.—An intoxication is a result of an insufficient intermediate metabolism associated with an acidosis. The damage to carbohydrate metabolism shows itself by an alimentary glycosuria; this disturbance is increased by hunger and loss of alkalies by a diarrhea.

Formerly it was asserted that intestinal stagnation produced a toxic agent of bacterial origin, but experimental observations show that food crystalloids cause fever and poisoning by physical osmosis. The thickening of blood is also of great importance.

Diagnosis.—Alimentary fever is distinguished from infectious fever by a therapeutic test, withdrawing food or by reduction of the whey and sugar in the mixture.

In a food intoxication the temperature falls by crisis unless the system is fatally damaged. In marasmus the patient may die of hunger with no sign of detoxication. Pure infections or infectious complications are not freed from fever by hunger metabolism.

Finally, with a very well-nourished child the detoxication may be slow and incomplete. (No explanation.)

Prognosis.—The outlook depends less on the severity of the symptoms than on the duration of the toxemia and on the previous condition of the child.

Prompt and correct treatment will cure most patients quickly. Thus, a baby who sickens on sweetened buttermilk may have threatening symptoms and very rapidly improve. A long period of intoxication is naturally exhausting. A marasmus baby will often die without relief.

Treatment.—With bad toxic symptoms the complete withdrawal of food cannot be avoided. Fluids should be freely supplied in the form of saccharin tea. To relieve the loss of fluid, salt solution is recommended. It has the disadvantage of sometimes causing fever. (Denied.)

Lavage of the stomach and intestine is useful, but not indispensable. Laxatives should not be used in diarrheal cases.

As stimulants, camphor, caffeine, digitalin, adrenalin, cognac, are well spoken of. High temperatures are to be combated by hydrotherapy. With a cold skin, hot mustard baths are effective.

With favorable, uncomplicated cases the starvation will, in twenty-four to thirty-six hours, cause a complete disappearance of the intoxication. The stools are less frequent; the baby is thin but placid. Feeding must now be commenced, at first in small but increasing amounts. Fluids must literally be pushed into the patient.

Human milk is the best food. The earlier the child is rescued from inanition the better; on the other hand, over-feeding will quickly produce a relapse.

Human milk may at first be given in a bottle; later the baby may be nursed.

If artificial food be used, the injurious fats and sugars should be avoided. Skim-milk, buttermilk are useful. The first doses should be 5 gm., five to ten times a day. The dietetic treatment is similar to that in dyspepsia.

Albumin milk is much used by Finkelstein. It has no tendency to ferment and can be digested in large quantities.

An emphatic warning is given, that mixed forms of intoxication and marasmus babies do not endure starvation, and after a few hours on tea they should be fed either human milk or albumin milk.

NUTRITIONAL DISTURBANCES IN BABIES FROM LACK OF FOOD

We see frequently the clinical picture of inanition and its consequences in children who have been given insufficient food on account of primary intestinal disturbances. Healthy babies or those who are only slightly ill respond to a considerable reduction in food by constipation and a loss in weight. If the underfeeding is continued the patient will have subnormal temperature and slow pulse.

The similarity of this condition with decomposition is unmistakable. At first, hunger inanition is distinguished from decomposition in that an increase in food brings up the weight quite rapidly, but finally the organism is so weakened that digestive tolerance is much reduced. This is observed in the convalescence from severe spastic pyloric stenosis after vomiting has ceased.

If the patient is given large quantities of food, even of human milk, it may lose in weight—a severe paradoxical reaction. A child dying of pyloric spasm sinks into a terminal toxic coma as in marasmus.

More frequently one sees bad consequences of inanition in severe disturbance of nutrition. Here food has been diminished or withdrawn far too long a time and without knowledge of the great danger.

With such children hunger and underfeeding has a terrific effect—a drop in weight, slow pulse, subnormal temperature, collapse and even death.

There is often a permanent weakening of digestion, so that the amount of food that is assimilated before the hunger period will now cause serious symptoms. In a severe case a short period of starvation gives the patient a strong push downward. A baby grows steadily weaker with moderate underfeeding, while repeated hunger periods result in a hopeless condition.

It may, therefore, be laid down as a fundamental principle in the prophylaxis and therapeutics of disturbances of nutrition that starvation and underfeeding can indeed remove toxic symptoms and fermentation of alimentary origin, but they may also cause far-reaching damage, and that this starvation treatment must be reduced to the minimum of necessity.

QUALITATIVE INANITION

This is a form of malnutrition in which the nourishment lacks important food elements and has an insufficient caloric value; as a result, the vitality is seriously damaged and poor tissue is formed.

The most common type of inanition occurs in babies fed largely or wholly on starchy gruels. The gruel has been prescribed to relieve diarrhea and has been continued by the mother. For a while the body shows no signs of illness, and may gain in weight from the retention of water in the tissues by the carbohydrate diet. The flesh is soft and pasty and the patient may have a muscular hypertonia—latent tetany.

1. The atrophic type is seen where starch gruel has been given without salt. It is distinguished from starvation inanition by the dryness of the tissue and the hypertonicity of the muscles.

2. The hydremic form is observed where the gruel has been salted and the weight is increased by water retention. The face is pale and swollen, the flesh is flabby and often edematous, without kidney irritation. Occasionally great muscular rigidity may be seen.

The stools vary with the carbohydrates—are foamy, mucous, liquid or solid; sometimes the patient has a colitis.

Wide fluctuations in the weight curve are characteristic.

If the child has a slight infection the weight may drop from several grams to a kilo. Purulent skin infection, inflammation of the cornea, conjunctiva, pneumonia or pyelitis may show the lessened resistance to bacterial infection.

The disturbances from the exclusive use of starch gruels result from the lack of essential tissue-building food elements—fats, albumin, salts. A serious consequence is the lowered production of antibodies and reduced immunity.

Prognosis.—The younger the baby and the longer the incorrect feeding has been carried out, the worse is the outlook.

Prophylaxis.—Qualitative inanition is prevented by a sensible diet, when starchy diet is ordered for therapeutic reasons to relieve convulsive symptoms or stop a diarrhea. The danger of starch inanition should be remembered with spasmophilia. Albumin preparations, fats and salts may be used. With a diarrhea, gruels should be used for only a short time without adding milk.

Treatment.—With very young babies human milk is best at first in minute doses. In general, whole milk should be added to gruel. Finkelstein advises albumin milk. The gruel should be gradually reduced, lest a terrific drop in weight occur.

476 Franklin Street.

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A CONTRIBUTION TO THE DIAGNOSIS AND PROGNOSIS OF CONGENITAL CARDIAC DISEASE *

CHARLES HUNTER DUNN, M.D.

Instructor in Pediatrics, Harvard Medical School; Physician to the Infants' Hospital

BOSTON

In 1901, in Vienna, I undertook as a special study the subject of congenital cardiac disease. It seemed to me that necropsies in which congenital cardiac lesions were found were so frequent, especially in the obstetric division of the general hospital, that there was a good opportunity to study these conditions by a comparison of the clinical and post-mortem findings. The number of cases which I had an opportunity to study in this way were in the end so few (thirty), that I have hitherto hesitated to publish the results of this investigation, and have waited until I should be able to add to my series of cases. This I have done, somewhat, from the records of the Infants' Hospital, although only comparatively few cases have been added, as we are able to obtain permission for so few necropsies. Since I began to do the hospital necropsies in 1907, a few cases of congenital heart lesions have been found, and by searching through all the hospital necropsy records, I have added eighteen cases to the original series, making forty-eight cases in all, of which I have satisfactory records.

One reason for presenting this subject is the fact that most text-books give a very confusing and unsatisfactory view of the diagnosis of the congenital cardiac lesions. The best books admit the difficulty of diagnosing the lesion from the clinical data presented, and describe the symptoms of the various lesions in a way which is of little help either in diagnosis, or as a basis for teaching students. Not only in the text-books, but also in the literature of congenital cardiac disease, is much confusion and contradiction to be found. I must confess, also, that some of the conclusions drawn from my own series of cases are not supported by the weight of evidence presented by the literature, which, of course, comprises a much greater number of cases. It is true that many of the statements as to the diagnosis of congenital cardiac disease, made even by men of high authority, do not seem to me to be justified by the evidence presented. Certainly many of the clinical descriptions are defective. The chief fault seems to me to be that fre-

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quently in the literature the symptom-complex seen in cases in which several congenital lesions are found is used as a basis for drawing conclusions as to the symptoms and signs of single lesions. Indeed, it is evidently the frequency of a combination of lesions which has led to so much uncertainty in diagnosis.

I have found that, in teaching students year after year, I have become more or less influenced in my teaching by the results of my own study of congenital cardiac disease. As my cases are still so few, I may be going hopelessly wrong. It is for this reason that I am presenting the cases at this time, for comparison with the views and experience of others, hoping to benefit by the criticism of the Section.

THE LESIONS FOUND POST-MORTEM IN FORTY-EIGHT CASES

The cases in my series in which a clinical diagnosis of congenital cardiac disease made before death was confirmed at autopsy are forty in number. There were eight additional cases, in which a congenital cardiac lesion was found at necropsy, but in which careful physical examination failed to give any evidence of a cardiac lesion, and four more cases in which the clinical diagnosis of congenital cardiac disease was made, but in which the heart and vessels at necropsy were found to be normal.

Of the eight cases in which there was no murmur or other clinical evidence, in all the lesion found was an open foramen ovale. In seven cases this was the only lesion. In one case there was, in addition, a small opening in the ventricular septum. The four cases in which the diagnosis was not confirmed at necropsy showed a systolic murmur as the only clinical evidence, there being no cyanosis, thrill, or enlargement of the area of cardiac dulness. One of these occurred this year at the Infant's Hospital, the clinical diagnosis being open ductus arteriosus.

In considering the various lesions found, the eight cases in which there were no clinical evidences of cardiac disease, in all of which open foramen ovale was the principal lesion, will be excluded. In the forty cases the various lesions were as given in Table 1.

TABLE 1.—LESIONS IN FORTY CASES OF CONGENITAL HEART DISEASES

Pulmonary stenosis alone	16 cases
Deficient ventricular septum alone	3 cases
Open foramen ovale alone	2 cases
Open ductus arteriosus alone.....	1 case
Congenital abnormality of the pulmonary artery....	1 case
Deficient septum with open ductus.....	9 cases
Deficient septum with pulmonary stenosis.....	7 cases
Pulmonary stenosis with open ductus.....	1 case

In this table open foramen ovale is not included, except in the two cases in which it was the only lesion. It was found as an associated lesion in quite a number of the cases, but I have omitted it, as including it in the various combinations would add greatly to the complexity of the combinations, and I believe it to have very little clinical significance.

Table 1 brings out at once a great discrepancy between my series of cases and the majority of the statements in the text-books and literature. The most prevalent opinion is that pulmonary stenosis is very rare alone, but is usually combined with some other lesion; yet in my series it was the sole lesion found in sixteen cases. It is interesting that all of these sixteen patients were babies who died very shortly after birth, some of them dying within a few hours, and none of them living more than three weeks. The cases all occurred in the obstetric division of the Vienna General Hospital. All of them were blue babies. There were three other cases of blue babies dying shortly after birth, and in all of them pulmonary stenosis was also found, but it was combined with other lesions.

It is further notable that in the twenty-one patients who survived a considerable time (of the case-reports, thirteen were collected in Vienna, and eight from the Infants' Hospital), there was no case of pulmonary stenosis as the only lesion. I believe that the discrepancy between my series and the statements of the literature may be explained on the ground that the latter are based mainly on cases of patients who lived a considerable time. Only in places like Vienna, where all babies dying in a large obstetric hospital are examined post mortem, can evidence as to these blue babies who die so shortly after birth be obtained. In other places, owing to the difficulty in obtaining necropsies, or to the lack of interest in the blue babies, comparatively few necropsies have been performed on this type of case, and conclusions have been based on the post-mortem findings of a later period of life. Necropsy findings are no measure of the clinical frequency of occurrence of a lesion, but rather of its fatality. I believe that the true conclusion should be, not that pulmonary stenosis alone is a rare lesion, but rather that it is a very fatal lesion, practically incompatible with life.

PULMONARY STENOSIS

To form any idea of the symptomatology of these various lesions, we must consider first the cases in which the lesion occurred alone. I shall not weary you with the exact statistics of the occurrence of each symptom and sign in each group of cases, but shall simply state the chief diagnostic points in the symptom complex. I shall omit from discussion in this paper all the symptoms and signs of congenital cardiac disease which have not immediately to do with the differential diagnosis of the various lesions. Such clinical features as malnutrition and defective development, or the clubbing of the finger-tips, and the blood-changes, associated with persistent cyanosis, will not be discussed. A murmur was present in all of the forty cases of the series, except one, and was always systolic in character, although in some

cases it continued through diastole. Therefore the cardiac murmur, in the various groups of lesions, will be taken for granted, and will not be mentioned unless it presented some special peculiarity. All of the cases in which pulmonary stenosis occurred as the only lesion showed a murmur systolic in character and cyanosis; ten cases showed a slight enlargement of the area of cardiac dulness to the right. The remaining six cases showed no evidence of such enlargement. In nine cases there was a distinct palpable systolic thrill. In two cases the thrill was reported as absent, and in five, its presence or absence was not recorded.

From mechanical considerations we should expect enlargement of the cardiac dulness in every case of pulmonary stenosis, and it is almost universally considered to be a necessary diagnostic sign of pulmonary stenosis. It is possible that its absence in six of my cases may be explained by the fact that some of the patients died within a few hours of birth, before there was time for enlargement to occur. It is to be regretted that my records do not include the exact duration of life in these early cases, so that I could compare it with the presence or absence of cardiac enlargement. Enlargement of the area of cardiac dulness was found in every one of the later cases in which pulmonary stenosis was combined with some other lesion. I believe enlargement of the area of cardiac dulness should be considered an essential diagnostic sign of pulmonary stenosis, although it may not be found in some cases in which death occurs shortly after birth.

I believe further, from these cases, that early death, or very brief survival after birth, should be considered an essential feature of pulmonary stenosis *alone*.

In eight cases, pulmonary stenosis was found associated with some other lesion. The lesion in seven cases was a deficiency, or opening in the interventricular septum of the heart, and in one case it was a patent ductus arteriosus Botalli. In all of these cases cyanosis was present, the systolic thrill was present, and enlargement of the area of cardiac dulness was present. In the single case in which pulmonary stenosis was combined with open ductus arteriosus, the murmur continued throughout the cardiac cycle, the so-called "humming top" murmur, and was very clearly transmitted into the great arteries of the neck, conditions which were not found in any of the other cases.

It would seem that the symptom-complex of pulmonary stenosis, so far as it bears on the differential diagnosis of the various lesions seen in congenital cardiac disease, consists essentially in three signs: cyanosis, cardiac enlargement and systolic thrill. As will be seen when we consider the signs found in the other lesion, cyanosis appears to be particularly associated with pulmonary stenosis. While all three of these signs are usually present, I believe a combination of cyanosis

with either of the others is sufficient for a diagnosis of pulmonary stenosis.

To determine whether pulmonary stenosis exists alone, or in combination with other lesions, is more difficult. From the findings in these cases I am inclined to the view that if a baby with the signs of pulmonary stenosis dies soon after birth, and from no intercurrent cause, it is most likely to be pulmonary stenosis alone; but in the blue babies which survive these early weeks, the lesion is pulmonary stenosis combined with some other lesion.

There is some theoretical support for this view. Several authorities have suggested that in pulmonary stenosis the existence of an open ventricular septum or ductus arteriosus is a helpful compensating condition, and not an additional source of disability. I am strongly inclined toward this view. Stenosis of the pulmonary orifice in a newborn baby introduces a very real mechanical obstruction to the circulation, one which conceivably may not be compatible with life, unless in some way compensated. Neither open ductus arteriosus nor open ventricular septum introduces any such mechanical obstruction to the circulation. On the contrary, they provide an additional means for the blood to pass from the right heart to the left, and thus may be a compensating factor in cases in which there is obstruction at the pulmonary orifice. Both lesions are developmental in origin, whereas pulmonary stenosis is regarded as due most frequently to fetal endocarditis. The pulmonary stenosis therefore may cause the developmental occurrence of compensating lesions. This view would explain the great fatality of uncomplicated pulmonary stenosis, and the combination of lesions in the babies which survived longer.

To determine the nature of the complicating or compensating lesion is, perhaps, farther than we can go, even in guessing. From the clinical findings of the eleven cases of open ductus arteriosus in this series, and from certain other cases diagnosed as open ductus, but not confirmed by necropsy, I should be inclined to guess as follows: If the murmur is particularly well transmitted into the great vessels of the neck, and especially if in addition the murmur is of the "humming top" variety, extending throughout the cardiac cycle, I should guess open ductus arteriosus. If these features were not present, I should guess deficient ventricular septum.

DEFECTIVE INTERVENTRICULAR SEPTUM

This was the commonest lesion found, being present in nineteen cases. In three cases this lesion was found alone. In none of these was there either cyanosis or palpable thrill. In all of them there was notable enlargement of the area of cardiac dullness. Thrill has been

described in these cases, but in most of the cases in the literature in which I found thrill mentioned, the lesion was associated with pulmonary stenosis, although there were some exceptions.

In nine cases it was associated with open ductus arteriosus. In these also there was no cyanosis, but a systolic thrill was present in two of them. Enlargement of the cardiac dulness was present in all of them. In six of these cases there was a notable transmission of the murmur into the vessels of the neck. In three this point was not recorded as either present or absent. In five cases there was a typical "humming top" murmur, extending throughout the cardiac cycle. In three cases the "humming top" murmur was recorded as absent, and in one case its character was not described. In none of the cases of deficient septum, except those associated with open ductus arteriosus, was noted either transmission of the murmur into the neck, or the "humming top" murmur.

In seven cases deficient septum was associated with pulmonary stenosis. They presented the clinical picture of pulmonary stenosis already described.

The essential diagnostic signs of defective interventricular septum appear to be murmur with enlargement, but without cyanosis. When there is neither transmission of the murmur into the vessels of the neck nor extension of the murmur throughout the cardiac cycles, the lesion may be diagnosed as existing alone. When these two signs are present, the lesion is almost certainly combined with open ductus arteriosus. When only transmission into the neck, without the "humming top" murmur, is present, the diagnosis of this combination is still probable. The combination of this lesion with pulmonary stenosis is diagnosed as described under that lesion.

OPEN DUCTUS ARTERIOSUS BOTALLI

This lesion occurred in eleven cases. In one case it was found alone, in one case associated with pulmonary stenosis, and in nine cases with defective interventricular septum.

In the case in which it was the sole lesion, there was no cyanosis, thrill or enlargement of the cardiac dulness. There were absolutely no other symptoms or signs of congenital cardiac disease than a systolic murmur transmitted loudly into the vessels of the neck. The patient died from an intercurrent tuberculous meningitis.

In the nine cases in which it was associated with deficient ventricular septum, the picture was that of defective septum, except for the presence in at least six of these cases of the transmission of the murmur into the vessels of the neck, for the presence in two of them

of thrill, and in six of them of the "humming top" murmur. The diagnosis of this combination has been already considered.

In the case in which open ductus arteriosus was found combined with pulmonary stenosis, the clinical picture and diagnosis have been already described.

It is interesting to note that the "humming top" murmur, conceded by most authorities to be the most important diagnostic sign of open ductus arteriosus Botalli, was absent in the one case of my series in which this lesion was found alone. We cannot of course conclude from this single case that this sign is not usually found when a persistent ductus arteriosus is the sole lesion. Indeed, if all the cases in which open ductus arteriosus was found at autopsy, alone, or in combination, are considered, we find that the "humming top" murmur was present in six cases, absent in four cases, not recorded in one case. The proper conclusion would be that the "humming top" murmur is frequently found in cases of open ductus arteriosus, but that it may be absent, and that its presence is not necessary for the diagnosis of this lesion. On the other hand, a "humming top" murmur was found in no case of congenital cardiac disease in which open ductus arteriosus was not present. Therefore this murmur, *when present*, may be considered diagnostic.

We can hardly draw conclusions as to the essential diagnostic signs of open ductus arteriosus from a series in which there was only one uncomplicated example of this lesion. We might conclude from this series that uncomplicated open ductus arteriosus is a very rare lesion. But we have already seen that the frequency of finding a lesion at necropsy is no measure of its frequency of occurrence in life, and if a fatal lesion, like pulmonary stenosis, can give a false impression of frequent occurrence, it is equally true that a benign lesion might give a false impression of infrequent occurrence. I believe that uncomplicated open ductus arteriosus is a very common lesion, perhaps the commonest of the congenital cardiac lesions, probably the commonest of the lesions compatible with survival. I base this belief on the frequency with which this symptom-complex, transmitted systolic murmur without cyanosis or enlargement, is encountered. This is the commonest picture of congenital cardiac disease met with in daily work in an infant's clinic. The essential features of these cases are the absence of other signs than the murmur.

I have records of thirty cases in which this clinical picture was found. Fifteen were taken from ten-years' records of ward cases at the Children's Hospital, and fifteen encountered in the out-patient department of the Infants Hospital between 1903 and 1912. These cases all showed the characteristic picture seen in the one which came

to necropsy. Nearly all showed the transmission of the murmur into the neck vessels, which appears to be the most important diagnostic sign of the lesion. A few showed a palpable systolic thrill. It is true that only ten of them showed the "humming top" murmur, and if this sign be considered necessary for the diagnosis of this lesion, there may be doubt as to the correctness of the diagnosis of open ductus arteriosus in the remaining twenty cases. But I have shown that this sign may be absent, and I believe the essential diagnostic features of this lesion are the presence of a murmur, without cyanosis or enlargement of the area of cardiac dulness, the murmur being transmitted into the vessels of the neck. Under this assumption, while there is no proof that these were actually cases of open ductus, it seems to me that the evidence points that way.

I have been able to follow, over a considerable period, fourteen of these cases. Eleven were Children's Hospital cases, taken from the records previous to 1903, and have been followed at least eleven years. The results in these were reported last year in a paper on cardiac disease. The other three were Infants' Hospital cases, and have not been followed so long. Of these patients, three died of some intercurrent acute disease while still in infancy, and eleven were well a year ago. The interesting feature of these eleven cases is that in all but three of them the murmur has disappeared. I cannot state the exact time of its disappearance, but in half the cases examined for the second time before the age of 4 years, the murmur had disappeared. These include four cases in which the "humming top" murmur was present.

It may be objected that these cases were not cases of congenital cardiac disease at all, especially as my records include four cases diagnosed as congenital cardiac disease, which showed no lesion at necropsy. None of these four cases, however, showed the transmission of the murmur into the vessels of the neck, whereas in most of the eleven cases followed to recovery, this sign was present.

I believe I am justified in considering these cases as open ductus arteriosus. If so, the evidence suggests that this is a benign lesion, tending toward complete recovery, and with no effect on health. It is notable that general development in my eleven cases of recovery was normal. Normally, the ductus is closed after birth by an obliterating endocarditis. Can we not conceive that its persistence, which is certainly of developmental origin, represents no more than a delay in the occurrence of the normal process of closure, and that the obliterating endarteritis may take place at a later period? This conception would explain the points which I have noted in these eleven cases of recovery, and would explain the infrequency with which this lesion is encountered at necropsy.

OPEN FORAMEN OVALE

This lesion was found at necropsy in two cases in which congenital cardiac disease was found during life. In one of these cases the clinical picture showed a murmur, being that of open ductus, except that the murmur was not transmitted into the neck. The other case showed slight cyanosis in addition to the murmur, without enlargement or thrill.

This lesion was encountered at autopsy in eight cases in which there was no murmur, nor other sign of cardiac disease. It was present also as a complicating lesion in quite a number of the other groups. It is a lesion which appears to have no clinical significance, and to be impossible to recognize clinically. It might be suspected in any case in which the clinical picture did not conform well to any of the recognized types, such as a case with cyanosis, but without thrill or enlargement, or a case with a murmur only, not transmitted into the neck.

CONGENITAL ABNORMALITY OF THE PULMONARY ARTERY

There was one case of this kind in my series. The baby showed marked cyanosis, and enlargement of the cardiac dulness to the right, but no thrill, and no murmur. It is interesting that this case was diagnosed practically correctly during life by Dr. Knopfmacher of Vienna, whose diagnosis was congenital hypoplasia of the pulmonary artery. He argued that the cyanosis and cardiac enlargement meant obstruction of the flow of blood through the lungs, but that the absence of either thrill or murmur meant that there could not be obstruction at the pulmonary orifice or at any other one point; therefore the whole pulmonary artery must be involved, as in hypoplasia. At necropsy one branch of the pulmonary artery was closed completely, and the other was much smaller than normal.

DIFFERENTIAL DIAGNOSIS

Table 2 shows the essential diagnostic features in the differential diagnosis of the various congenital cardiac lesions, as based on this series.

The following rules for differential diagnosis might be given:

1. A case showing cyanosis with enlargement of the cardiac dulness or palpable thrill, or both, is one of pulmonary stenosis. If the baby dies shortly after birth, the most probable lesion is pulmonary stenosis alone. If the baby survives early infancy, or lives on into childhood, the pulmonary stenosis is probably associated with some other lesion. If the murmur is notably transmitted into the vessels of the neck, or if a "humming top" murmur is present, the additional lesion is probably open ductus arteriosus. If the murmur has neither of these char-

acteristics, the complicating lesion is probably defective interventricular septum.

2. A case showing a murmur and enlargement, without cyanosis, is probably defective interventricular septum. If the murmur is not transmitted into the vessels of the neck, this lesion exists alone. If the murmur is so transmitted, or if the "humming top" murmur is present, the lesion is probably combined with open ductus arteriosus.

3. A case showing a murmur, without either cyanosis or enlargement, especially if the murmur is markedly transmitted into the vessels of the neck, or if it extends into diastole, is probably one of open ductus arteriosus alone. If the murmur is of the "humming top" variety, extending throughout the cardiac cycle, the diagnosis of this lesion is almost certain.

TABLE 2.—ESSENTIAL DIAGNOSTIC FEATURES IN THE DIFFERENTIAL DIAGNOSIS OF CONGENITAL CARDIAC LESIONS

	Cyanosis	Thrill	Enlarge- ment	Trans- mission of Murmur to Neck	Early Fatal Ending
Pulmonary stenosis alone	+	+	+	0	+
Defective interventricular septum alone	0	0 (occ. +)	+	0	0
Open ductus arteriosus alone	0	0 (occ. +)	0	+	0
Defective interventricular septum + open ductus arteriosus	0	0 (occ. +)	+	+	0
Defective interventricular septum + pulmonary septum	+	+	+	0	0
Pulmonary stenosis + open ductus arteriosus..	+	+	+	+	0

PROGNOSIS

The prognosis of the various congenital cardiac lesions and their combinations does not vary with the character of the lesions except in two forms, namely, pulmonary stenosis alone, and open ductus arteriosus alone. In all the other forms and combinations there is evidence that any patient may survive, and even live to adult life. On the other hand, the evidence shows that development and nutrition suffer to a varying degree, and that the children are in general less resistant, many of them dying young of various additional affections, such as the gastro-intestinal or infectious diseases. The prognosis in babies cyanotic at birth is grave, as many of them have pulmonary stenosis alone,

and die within a very short time. In those who survive, the pulmonary stenosis is probably combined with some compensating lesion, and is that of congenital cardiac disease in general.

In cases which show the clinical picture of open ductus arteriosus alone, the prognosis is very good. The patients do not usually show any interference with development or nutrition, but develop normally, with eventual disappearance of the signs of cardiac disease.

178 Marlborough Street.

EXPERIENCES WITH WHEY MODIFIED MILK IN INFANT FEEDING*

JEROME S. LEOPOLD, M.D.

NEW YORK

Human milk is unquestionably the milk of choice in infant feeding, but when human milk cannot be obtained artificial feeding must of course be employed. During the past few years many milk mixtures have been devised, and much progress has been made in artificial feeding. The *Eiweissmilch* of Finkelstein and Meyer^{1, 2} has been used extensively in all countries, and generally with very good results. The great drawbacks to its use are the complexity of its preparation, and the undesirability of employing it for prolonged periods. Heim and John,³ Feer,⁴ and recently Stoeltzner⁵ have so simplified the method of making it that *Eiweissmilch* can now be easily and cheaply made in private homes. Stoeltzner's method, consisting in adding a preparation of calcium-casein to one pint of milk and one pint of water is the simplest method. Bertlich,⁶ and also Wegener⁷ have recently treated a large number of infants with Stoeltzner's modification of *Eiweissmilch*. Their results are as favorable as those with Finkelstein and Meyer's original *Eiweissmilch*. The various constituents of this preparation are in nearly the same proportion as those in the original *Eiweissmilch*. (*Eiweissmilch* contains proteins 3 per cent., fats 2.5 per cent., sugars 1.5 per cent., salts 0.5 per cent.) *Eiweissmilch*, as is well known, is used in the treatment of nutritional disturbances of infants.

It was originally recommended for sick infants, and has rarely if ever been used as a food for well infants.

Keller's malt soup has been used extensively and with very good results for well and sick infants during short periods of time. The same may be said of buttermilk prepared in various ways. None of these milk mixtures, however, are useful for the nourishment of well babies over long periods.

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

1. Finkelstein, H., and Meyer, L. F.: *Jahrb. f. Kinderh.*, lxxii, Nos. 5 and 6.

2. Leopold, J. S.: *Arch. Pediat.*, August, 1910.

3. Heim and John: *Monatsh. f. kinderh.*, xi, No. 12.

4. Feer: *Jahrb. f. Kinderh.*, lxxviii, No. 1.

5. Stoeltzner: *München. med. Wchnschr.*, 1913, No. 6.

6. Bertlich: *Ztschr. f. kinderh.*, 1913, No. 9, p. 338.

7. Wegener, W.: *München. med. Wchnschr.*, 1914, No. 7.

Simple milk mixtures, top milk, etc., with the addition of cane, milk and malt sugars, and the various cereals have been used with very good results by many observers, but all are agreed that there is much room for improvement in the artificial feeding of infants for prolonged periods.

E. Schloss⁸ of Berlin in a recent monograph on infant feeding has described a new milk preparation designed for sick and well infants for long periods of time. A physiologist, Friedenthal, had previously prepared a milk which resembled human milk very closely. At first Schloss used this milk on a number of infants, but with not great success. He then modified Friedenthal's mixture, and as we shall see, obtained strikingly good results with this modification.

This milk preparation Schloss called "whey modified milk," because especial attention was given to the modification of the salts contained in the whey. He came to the conclusion that the reason infants do not do as well on cow's milk and its modifications as on human milk is because the percentage of the salts in the two milks is different. He therefore constructed his whey modified milk so that the proteins, fats, sugars and the salts contained in the whey should be in the same proportion as in human milk. In other words, Schloss endeavored to procure a milk mixture that should be in every respect as nearly identical as possible with human milk.

In a preliminary report⁹ I described the method of making Schloss' "whey modified milk," and published a summary of the cases treated with this preparation during one year. Quoting from this paper:

To make one liter of the mixture the following ingredients are used:

Twenty per cent. cream.....	140 c.c.
Full milk	140 c.c.
Water	700 c.c.
KCl	0.2 gm.

This mixture has the same percentage of salts and fats as human milk, but less protein and less sugar. To make up for this deficiency, casein is added in the form of nutrose or plasmon, and sugar is added in the form of a dextrin and a maltose preparation, because it has been shown that this preparation of sugar is better borne than milk or cane sugar. Schloss first tried milk sugar in his modification, but his results were not nearly as good as when dextrin and maltose were added. Furthermore, Schloss observed that his young infants made better progress if a small amount of flour was added to this mixture. Two mixtures were made, one containing flour, and one without flour. The mixture with flour is used for infants under 3 months, and is called mixture "A." The mixture without flour contains more sugar than mixture "A," and is used for infants over 3 months of age. This mixture is called "B."

8. Schloss, E.: Ueber Säuglingsernährung. S. Karger, Berlin, 1912.

9. Leopold, J. S.: Arch. Pediat., January, 1914.

Mixture "A." For infants under 3 months.

Twenty per cent. cream.....	140 c.c.
Full milk	140 c.c.
Water	700 c.c.
KCl	0.2 gm.
Dextrin and maltose.....	35 gm.
Flour	15 gm.
Nutrose or plasmon	5 gm.

Mixture "B." For infants over 3 months.

Twenty per cent. cream	140 c.c.
Full milk	140 c.c.
Water	700 c.c.
KCl	0.2 gm.
Dextrin and maltose.....	50-70 gm.
Nutrose or plasmon	5 gm.

If flour is used, it must be boiled with the sugar, casein preparation and water for fifteen minutes. If no flour is used, the mixture is simply brought to the boiling point.

The "whey modified milk" that has been described above was administered by Schloss to two hundred infants for a period approximating one year. About half of these infants were under 1 month of age, and the remainder were chiefly in the second month of life. The youngest infant was 8 days old. *None of the infants fed on this whey modified milk died from any nutritional disturbance.* One died of empyema, and one succumbed to an influenzal infection.

According to Schloss, all the infants took this feeding very well. The stools were, as a rule, yellow, homogeneous, and of a pasty consistency. The reaction was usually alkaline. At times, when the stools were dyspeptic on breast-feeding, changing to this whey modified milk resulted in normal stools. Vomiting was rarely observed, although this food contains a rather large percentage of fat. If vomiting occurred, it was easily cured by giving more frequent feedings—seven or eight—or even more instead of six in twenty-four hours. The infants showed a degree of physical development which in institutional children, at any rate, is only seen among those who are breast fed. In addition their sleep, color and muscular tone was all that could be desired.

Reinach¹⁰ of Munich has recently reported satisfactory results with Schloss' whey modified milk in both well and sick infants. No other reports have appeared either from abroad or in America. In a personal communication, Schloss has informed me that he has now used this milk mixture on about 800 infants with excellent results. It therefore seemed to me well worth while to report my additional experiences with it.

WHEY MODIFIED MILK

During the past two years I have used Schloss' "whey modified milk" in the feeding of 54 infants.¹¹ These were all institution babies. The great difficulty in bringing up institution infants on any method of artificial feeding is well known. I have observed about half of these

10. Reinach: Vortr. Geh. i. d. München. Gesellsch. f. Kinderh., abstract in Ztschr. f. Kinderh., ref. 1914, vii, No. 8.

11. At first owing to an error in our diet kitchen a higher percentage of fats than that recommended by Schloss was used.

cases for more than one year, and some of these for a year and a half. I have therefore been able to follow their general development over a rather long period. The ages of these infants varied from 2 days to 13 months; 16 were under one month of age; 24 between 1 and 3 months; 7 between 3 and 6 months; 7 over 6 months. None of the infants was suffering from severe enteritis when given this milk, but many of them were poorly nourished and underdeveloped, and some were suffering from an attack of influenza (grip) (which, as is well known, is very prevalent in institutions). There were 15 atrophic babies among my cases. None of the infants who received this milk mixture suffered from any gastro-intestinal disturbances while on this feeding. There were two fatalities among my cases, one from a severe influenzal infection complicated by double otitis media, and one from streptococcus peritonitis. It should be stated, however, that these deaths bore no relation to the milk feeding; both infants were well nourished at the time they became ill.

METHOD OF ADMINISTERING WHEY MODIFIED MILK

The milk was given in the same amounts as breast milk. (Both contain about the same number of calories.) In a few cases whey modified milk was administered in combination with breast milk with very good results. We usually gave six feedings in twenty-four hours, and rarely more than 1 quart of milk during that time. Almost invariably the infants took this feeding very well. Whey modified milk looks like any ordinary milk mixture, and has a pleasant taste. If vomiting occurred, an increase in the number of feedings (eight or more in twenty-four hours, as suggested by Schloss) nearly always controlled it, unless the vomiting was a symptom of some organic affection. If anorexia developed, as it did at times, and especially in infants suffering from influenza, the increase in the number of feedings nearly always improved this condition as well.

The stools after whey modified milk had been given for a few days generally had an alkaline reaction, were yellow in color and had the homogeneous, pasty consistency described by Schloss. With no other feeding except perhaps breast milk were such good stools obtainable. In infants a few days or weeks old, the stools were at times acid in reaction and contained small amounts of mucus for a few days. If the stools remained rather loose, the addition of a few grams of plasmon to the day's feeding usually caused yellow, homogeneous stools. There were rarely more than two to three movements in twenty-four hours. Constipation was rarely observed on this feeding.

Gain in Weight.—Schloss' whey modified milk is especially indicated in very young infants, and in infants under 6 months of age.

As a rule, these infants gained steadily in weight unless suffering from influenza. At times, if the weight curve remained stationary for a few days, the addition of a tablespoonful or more of malt sugar to the day's feeding resulted in a gain in weight. Infants over 6 months of age do not seem to do so well on this feeding. Their stools remain good, but it is very difficult to obtain a satisfactory gain in weight. Schloss' milk is therefore not indicated for infants in the second half year of life. As my weight curves and case reports show, the gain in weight was a gradual one. There were no enormous gains such as one frequently sees on a food rich in carbohydrates (and which, as is well known, is due to a retention of water, with a corresponding loss of weight in a few days). In the favorable cases unless complications, such as an attack of influenza, arose, a steady gain of 4 to 6 ounces each week was seen on whey modified milk. During an attack of influenza without any rise in temperature the weight curve may remain stationary for weeks at a time even on breast milk. The frequency with which influenza has affected my cases will not seem strange when one considers that L. F. Meyer¹² has recently shown that during the first thirty days' stay of an infant in an institution it suffers one attack of influenza, and during 100 days it has, as a rule, three such attacks. Loss of weight was very rarely observed among my cases.

It should be stated that all infants did not do well on this feeding. In a few cases the weight curve remained stationary, and anemia and malaise developing, breast milk was substituted.

General Condition of the Infants.—The general condition of the infants who received whey modified milk was, as a rule, excellent. They were well nourished and cheerful. Their skins remained free from infection. The color was good, and the subcutaneous tissue of the body became or remained firm and healthy. A study of the individual histories will show that the subsequent development of babies on whey modified milk was all that could be desired.

SUMMARY

Of the 54 infants who received whey modified milk very good results were obtained in 36 cases, fairly good results in 10 cases and poor results in 8 cases. The following infants did not do well on whey modified milk; 2 cases in infants over 6 months of age, 2 cases of atrophy, 1 case of exudative diathesis, 1 case of influenza, 1 case of enteritis and 1 case of nervous vomiting.

Below are the histories of the 54 infants who received whey modified milk. My cases were, as a rule, well infants. However, I see no

12. Meyer, L. F.: *Hospitalismus*. S. Karger, Berlin, 1913.

reason why this milk mixture should not be administered to infants suffering from nutritional disturbances.

Based on the results obtained by me while using Schloss' whey modified milk during a period of two years the following conclusions seem warranted:

CONCLUSIONS

1. Whey modified milk is indicated whenever breast milk is not obtainable.

2. Much better results are obtained with this milk mixture than with any other method of artificial feeding, in institutions at any rate.

3. Whey modified milk is especially indicated in very young infants, and in infants under 3 months of age.

CASE REPORTS (GOOD RESULTS)

CASE 1.—Infant 3 months of age. Weight, 6 pounds 5 ounces. Pale, poorly developed infant. Received breast milk for three weeks, and gained 1 pound during that time. It was then given a simple milk dilution with malt sugar for a little over one month, and gained about 2 pounds. The infant then developed an attack of influenza with a rise in temperature to 101 F., and there was a loss of 1 pound in two weeks. Whey modified milk was then substituted and a gain in weight resulted at once. During the first month there was a gain of 2 pounds and 11 ounces. During the next five weeks there was a gain of 1½ pounds. The infant was then put on a mixed feeding, and has done very well ever since. At 17 months it has eight teeth and weighs 18 pounds. It has good color and its general condition is excellent. There are no signs of rachitis.

CASE 2.—Infant 2 months of age. Weight 9 pounds 12 ounces. Pale child, fairly well nourished. Given a simple milk dilution for nine days and gained 2 ounces. It was then given whey modified milk for twelve weeks and gained 3 pounds 4 ounces, a weekly gain of nearly 4½ ounces. It was put on a milk dilution and has done fairly well. At 11 months it weighs 17½ pounds. It has good color and looks very well.

CASE 3.—Infant 5 months of age. Weight 9½ pounds. Underdeveloped. General condition fair. Has an attack of influenza. Received whey modified milk for twelve weeks and gained 4 pounds 12 ounces, an average weekly gain of over 6 ounces. It then received a simple milk mixture and has done fairly well. At 1 year infant weighs 19 pounds. It has four teeth and its general condition is excellent.

CASE 4.—Infant 6 months of age. Weight 7 pounds 10 ounces. Very poorly developed infant. Infant was given a simple milk mixture for four weeks and gained only 6 ounces during this time. It was then given whey modified milk for five days without any gain in weight. It was then put back on a simple milk mixture and in less than two weeks there was a gain of 1 pound. It was then given Schloss milk for about two weeks, during which time the infant had a severe attack of influenza. Ear paracentesis was done. In spite of this there was a gain of 12 ounces during this time. Infant was then put on breast milk and gained 8 ounces in two weeks. Then put back on Schloss milk. In fourteen weeks there was a gain of 4 pounds, an average of about 5 ounces each week. It was then put on a simple milk mixture and developed influenza, and lost 8 ounces during the next four weeks. It was then put on Schloss milk and immediately started gaining. There was a gain of 12 ounces during the first week. During ten weeks the infant gained 4 pounds, or about

7 ounces each week. It was then given whole milk, etc. At 18 months it weighs 22 pounds, has fourteen teeth and its general condition is excellent.

CASE 5.—Infant 3 months of age, 9 pounds 2 ounces in weight. Very pale, thin, underdeveloped infant. Stomatitis. Given Schloss milk for four weeks and gained 2 pounds during this time, or 8 ounces each week. It was then given diluted milk for three weeks during which time the infant only gained 5 ounces. It was then put back on Schloss milk and started gaining at once. During five weeks there was a gain of 2 pounds, or over 6 ounces each week. It was then put on various milk mixtures and has done fairly well. At 1 year of age infant weighs 19 pounds and looks very well.

CASE 6.—Infant 8 months of age, 9 pounds 10 ounces in weight. Pale, very poorly nourished infant. General glandular enlargement. Very nervous child. Given a simple milk mixture with cereal, etc., for three weeks, during which time there was a gain of 9 ounces, or 3 ounces each week. It was then given Schloss milk. During the first week there was a gain of 5 ounces. During thirteen weeks, although the infant had an attack of influenza during this time, it gained 5 pounds, or more than 6 ounces each week. The infant then developed a severe case of influenza with pharyngitis and otitis media, and a temperature of 103 F. For six weeks there was no gain or loss and the stools remained good. When the infant was convalescent it began to gain on a regular diet of full milk, etc. At 22 months the infant weighs 17 pounds 4 ounces and has fourteen teeth. Its general condition is excellent. This is a case of an older infant very much below normal in weight who gained very well on Schloss milk.

CASE 7.—Infant 4 months of age. Weight 12 pounds. Fairly well developed infant. Received a simple milk mixture for five and one-half weeks and gained 1 pound 2 ounces during this time, and then stopped gaining. It was then given Schloss milk and gained 8 ounces the first week. It then developed influenza with otitis media, and lost 16 ounces during the next eight days. Two ounces of breast milk was then given with each feeding of Schloss milk. The loss in weight stopped at once. Breast milk was given for three days, and then Schloss milk alone. During the next four weeks there was a gain of 21 ounces, or more than 5 ounces each week. The infant suffered another attack of influenza and during the next seven and one-half weeks there was a gain of only 8 ounces, but the stools remained good during this time. The infant was given a simple milk mixture with malt sugar at 9 months. During the first three weeks on this feeding it gained only 8 ounces, and for the past two weeks the weight curve has remained stationary. At 10 months the infant weighs 15 pounds.

CASE 8.—Infant 9 months of age. Weight 14 pounds. Fairly well nourished infant. Received a simple milk mixture and developed a severe alimentary intoxication. Lost $1\frac{1}{4}$ pounds in two weeks. Under appropriate treatment gradually recovered. After an interval of nine weeks infant gained 8 ounces. It was then given Schloss milk. During a period of eight weeks it gained on an average $8\frac{1}{2}$ ounces each week. It was then given malt soup for two weeks during which time there was no gain. It was then put back on Schloss milk and gained 12 ounces in two weeks. At 21 months of age it weighs 25 pounds and has four teeth. Its general condition is excellent. This was an older infant which gained nicely on Schloss milk.

CASE 9.—Infant 1 month of age. Weight $9\frac{1}{2}$ pounds. Well nourished infant. Has a rather severe stomatitis aphthosa. On Schloss milk during a period of four weeks it gained 1 pound 5 ounces, about 5 ounces each week. It was then put on a simple milk mixture for two weeks and gained 5 ounces, $2\frac{1}{2}$ ounces each week. It was then put back on Schloss milk and during two and one-half weeks it gained on an average 6 ounces each week. It then developed influenza and stopped gaining. Several milk mixtures were tried, but the infant did not do well until it was given breast milk. At 11 months the infant weighs 18 pounds 4 ounces, has four teeth and looks very well. Its general condition is excellent.

CASE 10.—Infant 10 months of age. Weight 15 pounds 2 ounces. Well developed infant. Received whole milk for six weeks, during which time there was a gain of $1\frac{1}{2}$ pounds, or 4 ounces each week. Infant then developed influenza with otitis media. There was a loss of 14 ounces in four days. It was then given Schloss milk. The loss in weight stopped at once. After two days the infant began to gain. In 5 weeks there was a gain of 28 ounces, or over 5 ounces each week. It was then given a regular diet and has done nicely ever since. At 1 year the infant weighs $17\frac{1}{2}$ pounds. At 2 years it weighs 22 pounds and is in excellent condition.

CASE 11.—Infant 6 months of age. Weight 10 pounds 2 ounces. Small, poorly developed infant. For two weeks previously the infant had received a simple milk dilution with malt sugar with no gain in weight. It was then given Schloss milk and gained nearly 2 pounds in less than three weeks. The infant then had an attack of influenza. During the next seven weeks while suffering from influenza the infant gained $1\frac{1}{2}$ pounds. It was given mixed feeding at 9 months. At 1 year the infant is in good condition and weighs almost 17 pounds. At 18 months the infant weighs $21\frac{1}{2}$ pounds, it has sixteen teeth, and its general condition is very good.

CASE 12.—Infant 2 months of age. Weight 6 pounds 12 ounces. Very poorly nourished child with stomatitis aphthosa. Was given Schloss milk for six weeks, during which time it gained 1 pound 10 ounces, or over 4 ounces each week. It then received a simple milk mixture for two weeks and gained 8 ounces and the weight curve then remained stationary. Schloss milk was then given for three weeks during which time there was a gain of nearly 7 ounces each week. Infant then developed a severe case of influenza and weight remained the same. After influenza attack was over the infant gained nicely on a simple milk mixture. At 11 months it weighs $17\frac{1}{2}$ pounds and is fairly well developed.

CASE 13.—Infant 1 month of age. Weight 7 pounds. Poorly nourished infant. Sprue. General condition very poor. Received Schloss milk for $6\frac{1}{2}$ weeks, and gained 2 pounds during that time, or 5 ounces each week. Infant was then given a simple milk mixture for one and one-half weeks, and gained 4 ounces during that time. Infant then developed influenza. It was given Schloss milk for $2\frac{1}{2}$ weeks and gained 8 ounces during that time. The influenza became worse and infant lost steadily in weight on Schloss milk and other milk mixtures that were given. Death finally resulted from a broncho-pneumonia.

CASE 14.—Infant 3 weeks of age, 4 pounds 6 ounces in weight. Very small, atrophic, premature infant. Umbilicus still moist. Breast fed until admission. Received Schloss milk for one week and gained 10 ounces during that time. It was then taken away from the institution for three weeks and lost 6 ounces during that time. It was then given a simple milk mixture for eighteen days and gained 8 ounces. On Schloss milk for the same length of time it gained 10 ounces and its general condition was much improved. It was then given a simple milk mixture on which the infant has done fairly well. At 7 months it weighs 13 pounds and looks very well.

CASE 15.—Infant 11 days old. Weight 7 pounds 14 ounces. Well developed infant. Received part Schloss milk and part breast milk for one month and gained $1\frac{1}{2}$ pounds during that time. Then received Schloss milk alone for two weeks and gained 10 ounces. On a simple milk mixture during nine days there was a gain of only 4 ounces. Infant was put back on Schloss milk and gained 18 ounces in two weeks. Infant then developed influenza with double otitis media. During the next ten days there was a loss of 6 ounces. Infant was then put on simple milk mixtures and has not done very well. At 11 months infant weighs $13\frac{1}{2}$ pounds and has a slight grade of rachitis.

CASE 16.—Infant 3 months of age. Weight 11 pounds. Fairly well developed infant. Had been on various milk mixtures including malt soup and had only gained $1\frac{1}{2}$ pounds in ten and one-half weeks, or less than $2\frac{1}{2}$ ounces each

week. Infant was then given Schloss milk and gained $1\frac{1}{2}$ pounds in $5\frac{1}{2}$ weeks, or more than 4 ounces each week. It then developed influenza with double otitis media and gained only 1 pound during the next ten weeks. It was then put on a simple milk mixture and its weight has remained stationary for the past eleven days.

CASE 17.—Infant 5 weeks of age. Weight 5 pounds 9 ounces. Very poorly developed infant. Stomatitis, umbilical hernia, eczema. Received Schloss milk for one week and gained 8 ounces during that time. Influenza then developed and the infant was given breast milk at once. It has done fairly well on this feeding.

CASE 18.—Infant 4 weeks of age. Weight 10 pounds 3 ounces. Very well developed infant. Received Schloss milk for twenty-four days, and gained an average of more than 6 ounces each week on this feeding. Infant then received malt soup for two weeks and lost 4 ounces. It was then put back on Schloss milk. In a little more than two weeks infant gained 1 pound. It then developed influenza with otitis media and weight remained stationary for four weeks. It was then given various milk mixtures including malt soup, but has not done well on any of these mixtures. At 11 months the infant weighs $14\frac{1}{4}$ pounds.

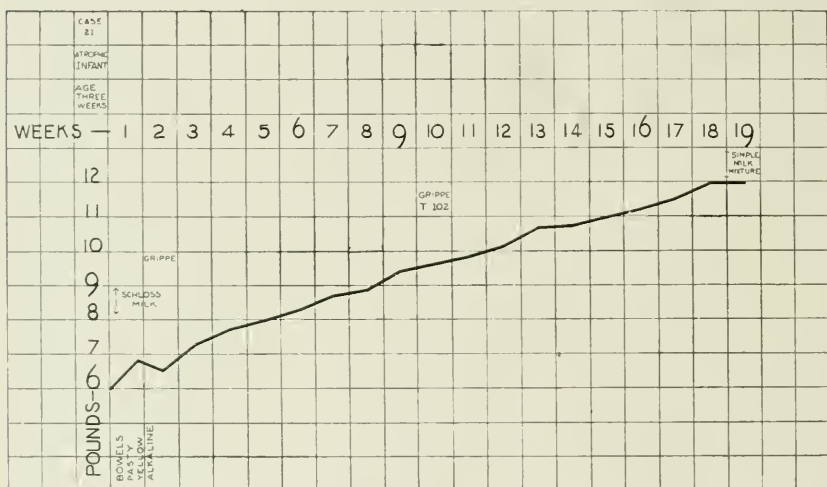


Chart 1, Case 21.

CASE 19.—Infant 3 weeks of age. Weight 8 pounds 10 ounces. Well developed infant, good color. Infant received a simple milk mixture for almost five weeks, and gained 20 ounces during that time, or almost 4 ounces each week. Infant was then given Schloss milk. During eleven weeks there was a gain of almost 4 pounds, or over 6 ounces each week. It then developed influenza and during six weeks it gained only 1 pound. It was then given a simple milk mixture, and in one week there has been a loss of 5 ounces. The infant is well developed and has good color.

CASE 20.—Infant 2 months of age. Weight 10 pounds 12 ounces. Well developed infant. Received a simple milk dilution for four days and gained 2 ounces. Infant was then given Schloss milk for eight weeks during which time it gained 2 pounds and 4 ounces, or $4\frac{1}{2}$ ounces each week. Its general condition is excellent and its color very good.

CASE 21.—Infant 3 weeks of age. Weight 6 pounds. Very poorly developed, atrophic infant. Has slight attack of influenza. Received Schloss milk for

eighteen weeks and has gained 6 pounds during that time, an average weekly gain of more than 5 ounces. The general condition is excellent and the color very good. Infant looks like a breast fed baby. Infant has been getting a simple milk dilution for the past three days with no gain in weight.

CASE 22.—Infant 3 months of age. Weight 8 pounds 11 ounces. Pale, poorly developed infant. Received simple milk mixtures for two months and gained nearly 2 pounds during that time. Infant then developed an intestinal intoxication. In four weeks there was a loss of $1\frac{1}{4}$ pounds. Infant was then given Schloss milk and loss in weight stopped at once. In ten days there was a gain of 12 ounces. Breast milk was then given for sixteen days with a gain of nearly 1 pound during that time. Then infant was given Schloss milk alone on which it gained fairly well until it developed influenza. At 17 months the infant weighs 20 pounds, it has four teeth and its general condition is very good.

CASE 23.—Infant 6 weeks of age. Weight 8 pounds 5 ounces. Fairly well developed infant. Exudative diathesis. Stomatitis. Received Schloss milk for ten weeks. During the first two weeks the infant had a rather severe stomatitis with dyspeptic stools, and there was very little gain in weight. During the next

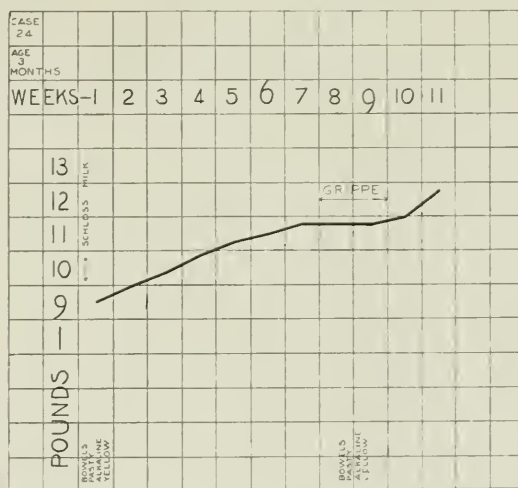


Chart 2, Case 24.

eight weeks the infant gained nearly 2 pounds, or about 4 ounces each week. It was then given a simple milk mixture on which it has done very well.

CASE 24.—Infant 3 months of age. Weight 9 pounds 8 ounces. Pale infant, fairly well developed. During a period of seven weeks while on Schloss milk infant gained 36 ounces, or more than 5 ounces each week. It then developed influenza and for two weeks there was no gain. During the next two weeks there was a gain of 16 ounces, or 8 ounces each week. During the attack of influenza the stools remained good.

CASE 25.—Infant 3 months of age. Weight 7 pounds 1 ounce. Marasmic infant. Pale. Very poorly developed. Severe stomatitis. Received Schloss milk for nine weeks and gained 2 pounds 10 ounces during that time, an average weekly gain of more than $4\frac{1}{2}$ ounces. The infant's stools which were dyspeptic on admission became homogeneous after a few days.

CASE 26.—Infant aged 2 months. Weight 9 pounds. Fairly well developed infant. Received Schloss milk for sixteen days and gained on an average about

4 ounces each week. A simple milk mixture was then given on which infant has done very well.

CASE 27.—Infant aged 2 weeks. Weight $6\frac{1}{2}$ pounds. Pale, very well developed infant. Received Schloss milk for $13\frac{1}{2}$ weeks and gained 3 pounds during that time, or nearly 4 ounces each week. At the end of this time the infant's general condition was excellent.

CASE 28.—Infant aged 7 days. Weight 6 pounds 1 ounce. Fairly well developed infant. Received Schloss milk for twelve and one-half weeks and gained 56 ounces during that time, or $4\frac{1}{2}$ ounces each week. Bowels have always been good.

CASE 29.—Infant aged 6 weeks. Weight 5 pounds 4 ounces. Very atrophic infant. Subnormal temperature. Very poorly developed. During a period of four and one-half weeks on Schloss milk there was a gain of 1 pound 13 ounces, or about 7 ounces each week. The bowels have always been homogeneous (as in nearly all of the cases), and the infant's general condition has improved wonderfully.

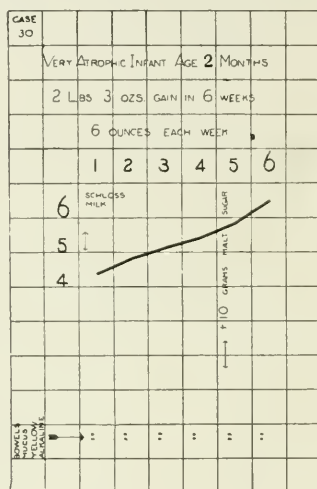


Chart 3, Case 30.

CASE 30.—Infant aged 2 months. Weight 4 pounds 7 ounces. Very atrophic, poorly developed infant. Received Schloss milk for six weeks and gained 2 pounds 3 ounces during that time, or nearly 6 ounces each week.

CASE 31.—Infant aged 7 weeks. Weight 5 pounds 10 ounces. Very atrophic infant. Subnormal temperature. Diffuse bronchitis. Received Schloss milk for nine weeks and three days, and gained 2 pounds and 10 ounces during that time, or over 4 ounces each week. The stools have always been good. The general condition has improved wonderfully.

CASE 32.—Infant aged 3 months. Weight 10 pounds 1 ounce. Fairly well developed infant. Received Schloss milk for eight days and gained 6 ounces during that time. Infant then developed influenza with a severe pharyngitis. During the next six weeks while infant had influenza there was no gain. After the attack of influenza had subsided the infant began to gain again. During the next two weeks there was a gain of $\frac{1}{2}$ pound. The infant was then given a simple milk mixture on which it is gaining slowly.

CASE 33.—Infant aged 1 month. Weight 8 pounds 10 ounces. Atrophic infant. Very poorly developed. During the first two weeks on Schloss milk

there was no gain in weight, although the stools were good and the general condition of the infant improved. Breast milk was then given in addition to Schloss milk for two and one-half weeks, during which time there was a gain of 1 pound. Schloss milk was then given alone, and during the following two weeks there has been a gain of 1 pound, or 8 ounces each week.

CASE 34.—Infant aged 13 months. Weight 13 pounds. Poorly nourished infant. During the past week infant had a severe enteritis and lost 1 pound in weight (on *Eiweissmilch*, and then on breast milk). Infant then received Schloss milk, in addition to breast milk, and at once a gain in weight resulted. During three weeks there was a gain of 1 pound and 5 ounces. Schloss milk was then given alone for four weeks and during that time there has been a gain of 1 pound and 5 ounces. The stools have been good since Schloss milk has been given.

FAIRLY GOOD RESULTS

CASE 35.—Infant aged 3 weeks. Weight 8 pounds 6 ounces. Well developed infant. Received Schloss milk for ten weeks and three days. During that time there was a gain of 2 pounds and 6 ounces, or an average of about 4 ounces each week.

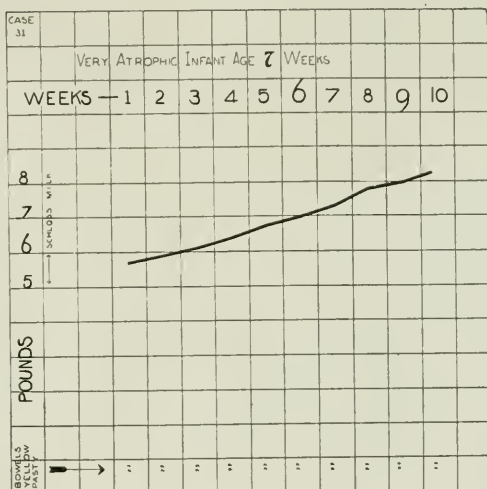


Chart 4, Case 31.

CASE 36.—Infant aged 3 months. Weight 11 pounds 8 ounces. Well developed infant. During a period of four weeks on Schloss milk there was a gain of $1\frac{1}{2}$ pounds, or 6 ounces each week. The infant then developed influenza with temperature as high as 103 F. During the next month with influenza there was a gain of 4 ounces and the stools remained good. During the next ten weeks the infant had several attacks of influenza and gained only 1 pound and 6 ounces. The stools have always been good. At 6 months of age the general condition is very good. The weight is 14 pounds 10 ounces. The color is excellent. The infant is still receiving Schloss milk.

CASE 37.—Infant aged 3 months. Weight 14 pounds 8 ounces. Well developed infant with exudative diathesis. Received a simple milk mixture for three weeks and gained 6 ounces during that time. Infant was given Schloss milk for the same length of time and gained 11 ounces.

CASE 38.—Infant aged 10 months. Weight 14 pounds. Fairly well developed. Received a simple milk mixture for six weeks and lost 6 ounces during that time.

Schloss milk was then given for five and one-half weeks and the infant gained 1 pound. Then put on a mixed feeding and has gained steadily ever since.

CASE 39.—Infant aged 5 months. Weight 9 pounds 14 ounces. Infant received Schloss milk for two weeks and gained 6 ounces during that time.

CASE 40.—Infant 3 months of age. Weight 13 pounds. Pale, poorly developed infant. Received a simple milk mixture for six weeks and gained $1\frac{1}{4}$ pounds during that time. It then received Schloss milk for eleven days and gained 4 ounces. Infant then received a simple milk mixture again for six weeks and lost 6 ounces. Then Schloss milk was given for two weeks, during which time there was a gain of 9 ounces. A simple milk mixture was again given for three weeks with a gain of 12 ounces. Schloss milk was then given for five weeks, with a gain of 16 ounces. Infant was then given a mixed feeding on which there was very little gain. At 10 months the infant weighs a little less than 17 pounds. This was an older infant that did not do well on any artificial feeding.

CASE 41.—Infant aged 1 month. Weight 8 pounds 12 ounces. Pale, poorly nourished infant. Received a simple milk mixture for nine days and gained 10 ounces during that time. Schloss milk was then given for four and one-half weeks with an average gain of 4 ounces each week. A simple milk mixture was then given for four weeks during which time infant developed influenza and lost 2 ounces. Schloss milk was then given again for six weeks with a gain of only 11 ounces. (Influenza.) Finally breast milk had to be given. At 10 months the infant weighs $14\frac{1}{2}$ pounds. The general condition is good.

CASE 42.—Infant, aged $3\frac{1}{2}$ months. Weight 9 pounds. Pale, fairly well developed infant. Received a simple milk mixture for three weeks and gained 14 ounces. Then developed influenza and infant was given Schloss milk. In spite of its influenza there was a gain of 16 ounces in one month. During the next few days the temperature was 103 F., the bowels became loose and the infant developed a double otitis media. There was a loss of 12 ounces in 2 weeks. The infant's general condition became worse and death resulted.

CASE 43.—Infant aged 1 month. Weight 9 pounds 14 ounces. Well developed infant. Had always received breast milk. Schloss milk was given for nineteen days with a loss of 4 ounces during that time. On a simple milk mixture there was a loss of 4 ounces in two days. Breast milk was then given for two days and the infant's condition improved a good deal. Schloss milk was again given for nineteen days and a gain of 14 ounces resulted.

CASE 44.—Infant aged 2 days. Weight 5 pounds 7 ounces. Poorly nourished infant. Infant has received no nourishment since birth. Received Schloss milk for seven weeks and has gained 1 pound 5 ounces during that time. The bowels have always been good.

CASE 45.—Infant aged 1 month. Weight 4 pounds 7 ounces. One of triplets. Atrophic infant in wretched condition. Received Schloss milk for almost six weeks and gained 15 ounces during that time. The bowels have always been good and the infant's general condition has improved remarkably.

CASE 46.—Infant aged 1 month. Weight 4 pounds 3 ounces. Marasmic infant. Looks very badly. One of triplets. Received Schloss milk for three weeks, and Schloss milk and breast milk for three weeks. During this time there has been a gain of 13 ounces. The infant's general condition has improved a great deal.

POOR RESULTS

CASE 47.—Infant 13 months of age. Weight 13 pounds 8 ounces. Very poorly developed infant. On a regular diet infant lost 1 pound in three weeks. It was then given Schloss milk for seven weeks and gained only 4 ounces. Then received malt soup on which it did not do very well. At 2 years of age the infant weighs only 17 pounds. The above described infant took all arti-

ficial feeding poorly, including Schloss milk. (As a rule infants over 6 months of age do not do well on Schloss milk.)

CASE 48.—Infant 12 months of age, 12 pounds 7 ounces in weight. Very poorly developed infant. Infant lost 1 ounce during a period of three months while on a regular diet. It was then given Schloss milk for five weeks and lost 10 ounces. It then developed influenza and enteritis. It was then given *Eiweissmilch* and has gained slowly on this. At 18 months infant weighs only 14 pounds. This infant was an older child which did not do well on Schloss milk.

CASE 49.—Infant 3 months of age. Weight 8 pounds 12 ounces. Poorly developed, pale, atrophic infant. During a period of three weeks, on Schloss milk, there was no gain. Infant was then given malt soup, etc., and Schloss milk was again tried, but on none of these mixtures was a favorable result obtained. On the malt soup the infant developed enteritis. At 12 months the infant weighs 15 pounds and has signs of rachitis. This was an atrophic infant that did not do well on Schloss milk.

CASE 50.—Infant 4 months of age. Weight 7 pounds 15 ounces. Very atrophic infant with exudative diathesis. Received Schloss milk for four weeks and gained only 5 ounces during this time. Then various milk mixtures were tried. Infant has done poorly on all feedings. Schloss milk was given again when infant was 10 months of age. During a period of five weeks there was no gain, nor could a gain be obtained on other feedings for the next two months. At 1 year the infant weighs 13 pounds 2 ounces and has marked signs of rachitis.

CASE 51.—Infant 1 month of age. Weight 7 pounds 4 ounces. Poorly developed infant with exudative diathesis. Suffering from influenza. Received a simple milk mixture for two and one-half weeks and gained 6 ounces during that time; infant was then given Schloss milk for twelve days and gained 5 ounces. Then received a simple milk mixture for four days and lost 6 ounces. Schloss milk was given again for two days and a gain of 6 ounces resulted. Simple milk mixtures and malt soup were tried for various periods of time, but on all of these the infant has done poorly. This was a case of exudative diathesis which did not do well on any artificial feeding.

CASE 52.—Infant 2 months of age. Weight 9 pounds 4 ounces. Pale infant. Fairly well developed. Suffering from influenza, otitis media. (Temperature as high as 104 F.) Received Schloss milk for seven weeks and gained only 8 ounces during that time. Stools always contained mucus and were acid in reaction.

CASE 53.—Infant 1 month of age. Weight 9 pounds 2 ounces. Pale infant. Well developed. Received Schloss milk for nearly three weeks. During this time the stools were yellow and pasty. The infant vomited a little after each feeding. There was a loss of 2 ounces during this time. The infant was then given a simple milk mixture for three days. The vomiting continued and the infant looked badly and there was no gain in weight. Breast milk was then given in addition. The vomiting stopped almost at once, but there was very little gain in weight. In twelve days the infant gained only 4 ounces.

CASE 54.—Infant aged 6 weeks. Weight 8 pounds 7 ounces. Very poorly developed infant. Stools loose, watery (enteritis). During a period of five weeks and five days on Schloss milk there was a gain of only 1 pound. Since then breast milk and *Eiweissmilch* have been given, but the infant has not done well on any feeding.

701 Madison Avenue.

THE RELATION OF BOVINE TUBERCULOSIS TO EARLY TUBERCULOSIS IN CHILDREN *

T. C. McCLEAVE, M.D.

BERKELEY, CAL.

It is now generally conceded that infection with the tubercle bacillus is, in the majority of cases, an incident of early life, and that, regardless of the time of development of clinical symptoms, tuberculosis is, in its origin at least, essentially a disease of childhood. Unfortunately, however, the recognition of this fact has failed to effect, as yet, any wide-spread movement directed toward the prevention of this early infection, which is the fundamental problem of the antituberculosis campaign. This is not to say that there are not numerous agencies dealing with many different elements of the problem, but the sum total of their work is pitifully small when compared with the tremendous amount of effort and money expended in combating the disease in adults, much of which expenditure is, and will continue to be, wasted until it is diverted to basic preventive work among children.

It is the purpose of this paper to attempt to emphasize one very much-neglected phase of this subject. While all recognize that infection with tuberculosis in a very great proportion of cases results from exposure to other human cases, it is now also well established that, in a certain smaller proportion of cases, the disease is derived from tuberculous cattle; but strange to say, this knowledge not only makes but little impression on the laity, but also, so far as practical activity is concerned, is regarded with indifference by the greater portion of the medical profession. Indeed, I have even heard clinicians especially interested in tuberculosis deprecate any agitation of this subject on the ground that it tended to divert popular attention from the larger subject of human infection, apparently ignorant of the importance of this factor in the causation of the disease, or failing to appreciate how easily it should be controlled if only sufficient interest in it be aroused.

Formerly, tubercle bacilli from whatever source were considered as identical except for minor differing characteristics regarded as due to changes in environment. Klein very early pointed out certain differences between bacilli derived from bovine and from human sources, but it was not until 1896 that Theobald Smith clearly differen-

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

tiated the two types. Briefly, the bovine bacillus is usually shorter and thicker than the human, stains more uniformly and grows more slowly and sparsely on artificial culture mediums, with less acid production; but it is chiefly distinguished by its very much greater pathogenicity for animals, especially cattle and rabbits, which are with difficulty infected with human bacilli. The most reliable laboratory method, therefore, for determining the type of bacillus from any given source is by rabbit inoculation. If the rabbit develops a rapid generalized tuberculosis, the infecting organism is to be regarded as of the bovine type.

The recognition of the differences in the characteristics of the two varieties of bacilli naturally led to doubt as to the identity of the pathologic conditions produced by each, culminating in Koch's famous dictum, in 1901, that human infection with the bovine bacillus was so rare that tuberculosis in cattle was negligible in respect to the etiology of tuberculosis in man.

This view was revolutionary, but, being supported by so great authority, it was at once evident that the importance of the question demanded an accurate determination, and as a result of the immense amount of investigative study which has since been devoted to the problem, we are now in possession of data which enables us to speak with considerable certainty regarding many of the points involved.

These data have been derived from the work of the British Royal Commission on Tuberculosis, of the German Tuberculosis Commission and of numerous individual investigators. Without going too much into detail, their results may be summarized as showing conclusively, in so far, at least, as character of bacillus is concerned, that pulmonary tuberculosis is practically always human in type, although two lung cases yielding the bovine type of bacillus were found by the British commission. On the other hand, in children a considerable percentage of the abdominal, meningeal and bone and joint tuberculosis and tuberculosis of the lymph-glands has been shown to be of bovine origin.

The British commission investigated 108 cases and found 19 of bovine infection, as follows: 2 cases of pulmonary tuberculosis; 14 cases of abdominal tuberculosis and 3 cases of cervical lymphadenitis. The German Tuberculosis Commission examined 56 cases and in 6 found bacilli of bovine type.

Park and Krumweide, of the New York Research Laboratory, have themselves studied 478 cases (1912), and adding these to the reports of others, have tabulated some 1,511 cases. These give results as follows (quoting their tables):

TABLE 1.—HUMAN AND BOVINE TYPE OF BACILLUS IN 1,511 REPORTED CASES (PARK AND KRUMWEIDE)*

Diagnosis	16 Years and Over		5 to 16 Years		Under 5 Years	
	H	B	H	B	H	B
Pulmonary tuberculosis ...	778	3	14	..	35	1
Tuberculous adenitis, axillary or inguinal.....	3	..	4	..	2	
Tuberculous adenitis, cervical	36	1	36	22	15	24
Abdominal tuberculosis....	16	4	8	9	10	14
Generalized tuberculosis, all forms, including meninges	40	1	19	5	172	33
Tuberculous meningitis....	1	..	3	..	28	4
Tuberculosis of bones and joints	32	1	41	3	27	
Genito-urinary tuberculosis	22	1	2	..		
Tuberculosis of skin.....	10	3	4	6	2	
Miscellaneous cases	2	1	..	1	1	
Totals	940	15	131	46	292	76

Mixed or double infections, eleven cases.

* H means human; B, bovine.

TABLE 2.—PERCENTAGE INCIDENCE OF BOVINE INFECTION

Diagnosis	Adults 16 Years and Over Per Cent.	Children 5 to 16 Years Per Cent.	Children Under 5 Years Per Cent.
Pulmonary tuberculosis...	0.4	0.0	2.8
Tuberculous adenitis, cervical	2.7	38.0	61.0
Abdominal tuberculosis ...	20.0	53.0	58.0
Generalized tuberculosis (alimentary)	14.0	57	47.0
Generalized tuberculosis...	0.0	16	8.6
Generalized tuberculosis including meninges (alimentary)	0.0	0.0	66.0
Tuberculous meningitis (other than above).....	0.0	0.0	4.6
Tuberculosis of bones and joints	3.3	6.8	0.0
Tuberculosis of skin.....	23.0	60.0	0.0

In their own series, of the fatal cases in children under 5 years, 12.5 per cent. were bovine infections; while in the total series, 26 per cent. of all cases in children under 5 years were of bovine origin; 35 per cent. in children 5 to 16 years of age, and only 1.5 per cent. in individuals above 16 years of age. The tables also show the rarity of fatal tuberculosis due to bovine infection in those over 5 years old, but a very high percentage of abdominal tuberculosis and cervical lymphadenitis due to bovine bacilli.

Practically all authorities concur in the interpretation of these findings, though differing in their estimates of the relative importance of the two types of infection.

Dr. S. A. Knopf, in a recent personal communication, says: "I believe strongly in the transmission of tuberculosis from cattle. Laboratory, as well as clinical experiments, and the experiences of the past few years of American and European investigators, show conclusively that about 10 per cent. of tuberculosis in children is due to the bovine type of bacillus."

M. J. Rosenau, in a similar communication, states that "up to one-fifth or one-fourth of all cases of tuberculosis in infants and children are associated with the bovine bacillus."

In England, Delépine, from a very careful study of the question, concludes that "it is possible to say without fear of exaggeration that not less than 25 per cent. of the tuberculous children under 5 years of age suffer from infection of bovine origin."

A. P. Mitchell, in a study of 72 cases of cervical adenitis in children, occurring in Edinburgh and its immediate vicinity, found sixty-five cases yielding bovine bacilli and only 7 cases yielding human bacilli. Thirty-five of the bovine cases were in children under 5 years old, and the remaining thirty in children under 12 years old. Of the children 2 years old or under, 84 per cent. had been fed on raw cow's milk.

J. Frazer of Edinburgh, in 100 cases of bone tuberculosis in children, found bovine bacilli in 62 per cent., and human bacilli in 35 per cent. of the cases, while 3 per cent. yielded both types. As indicative of the probable source of infection in the bovine cases, 73 per cent. of these children were under 3 years of age and had been fed unboiled cow's milk. Conversely, of the cases showing a human type infection, 71 per cent. gave a history of exposure to other cases in their families.

Sims-Woodhead and other English investigators report similar findings, although percentages vary in different localities. Edinburgh shows a particularly high percentage of bovine infections. Similarly, in Germany, wherever the subject has been studied by the bacteriologic

method, the percentage of bovine cases has been found to be from 19 to 26.

Orth, to cite but one eminent German authority, believes that at least 10 per cent. of all tuberculosis in children is due to bovine infection, and estimates that there are 200,000 persons in Germany with bovine bacillus infections.

It is clear, then, if we accept the type of bacillus as the criterion of the source of infection, that bovine tuberculosis plays a highly important part in the production of human tuberculosis, particularly those forms of the disease which occur most commonly during childhood, and is by no means a negligible factor as claimed by Koch.

Not all investigators are agreed, however, that the type of bacillus, as so far determined, is a valid criterion of the total amount of bovine infection in man. Von Behring and his followers claim that the bovine bacillus is a very common cause of even pulmonary tuberculosis, maintaining that the infection occurs in very early life from the ingestion of bovine bacilli, which, it has been shown, may pass through the uninjured intestinal mucosa and reach the lungs by way of the mesenteric lymphatics and blood-stream, often leaving no abdominal lesions by which to trace their course. Bacilli so introduced into the body are believed to be capable of prolonged latent existence in the tissues, becoming active under favorable conditions even after many years, and in the meantime changing in type from bovine to human. This view has been strongly supported by Vallée, Calmette and many others, Calmette asserting, in 1905, that a majority of cases of pulmonary infection originated in this way.

In this country, Ravenel has been one of the warmest advocates of the theory of the possibility of this method of infection. He has shown experimentally that infection of the lungs may be so produced, and has, in at least one instance, succeeded in changing a typically human type of culture, by passage through calves, into one showing typical bovine characteristics. He believes that the dearth of direct experimental evidence of such change is due to technical difficulties in the way of inducing artificially and over a sufficient period of time, conditions analogous to those under which the transmutation of type is supposed to occur in the human body, and pertinently points out the fact that if the tubercle bacillus is unable to change its characteristics under variable environments, it therein radically differs from bacteria in general.

Von Eber, also, believes in transmutability of type, and claims to have been able, by passage through cattle, to produce from human cases a virulent type of bovine bacillus (from adults 36 per cent. and from children, 53 per cent.).

Another important question bearing on the problem of change of type arises from the apparently almost exclusive incidence of fatal tuberculosis of bovine origin in children below 5 years of age, and the rapid decline of all forms of bovine tuberculosis infection during the period of late childhood. It seems competent to inquire, since bovine infections constitute, as we have seen, so large a proportion of the tuberculosis of early life, what becomes of the bovine bacilli in those subjects who do not die, many of whom must surely later exhibit other forms of the disease. If bovine bacilli do not change their characteristics with the advance in age of their hosts, it would appear that they ought to be abundant in adults.

Though there exists some actual and much presumptive evidence to warrant a belief in variability of type, however, it must for the present be said that the weight of opinion is to the contrary; but it must also be conceded that, regardless of the ultimate solution of this problem, we have in the already proved statistics of demonstrable bovine infection in children, ample occasion to regard tuberculosis in dairy cattle as a very serious menace.

It is true that this statement is still controverted by some, but it can be shown that their adverse reasoning is, for the most part, based on clinical and not bacteriologic evidence. Thus, Medin, in a report on the autopsy findings in 7,630 children who died at the Stockholm Hospital from 1842 to 1911, during the first year of life, considered that in only 2 per cent of the cases was there evidence of primary intestinal infection, and that in the remaining 98 per cent. the infection was primarily in the lungs. He says in thirty years' experience he has never seen a case of tuberculosis which he could ascribe to the use of milk. Such evidence is fallacious, as no one is at the present time able to differentiate the types of infection clinically.

As bovine bacilli practically always gain access to the human body through the ingestion of contaminated milk or milk products, methods of prophylaxis must be directed toward the eradication of the disease from dairy herds (an economic and biologic problem too vast for more than mention here), but more especially must depend for success largely on measures designed to render milk from even tuberculous animals suitable for dietetic use.

The United States Bureau of Animal Industry estimates that at least from 20 to 30 per cent. of the dairy cows in the United States are tuberculous, and, while in certain areas the percentage is very much higher; these figures are probably fairly indicative of the prevalence of the disease in cattle throughout the civilized world.

Many tuberculous cows expel bacilli with their milk, and in a very much greater proportion, virulent bacilli are found more or less con-

stantly in the intestinal discharges; so manure, as the most common and practically a universal contaminant of milk, is perhaps the chief vehicle for the transmission of tubercle bacilli from cow to baby.

Certified milk, or what may be had in a few cities, an almost equivalent grade of milk, which is produced from efficiently tuberculin-tested cattle, under such rigid conditions of cleanliness as to almost altogether preclude manure contamination, is the only commercial milk which affords reasonable assurances of safety, and it should be obtained for little children whenever possible. Its cost of production is such, however, that it must remain a high-priced milk, beyond the reach of the great bulk of the population, and it cannot, therefore, of itself, have any very appreciable direct influence in the control of the spread of bovine infection to man. Recourse must then be had to methods which will render safe the ordinary grades of market milk. Dairy hygiene, unfortunately, in spite of high development in certain limited districts, is practically everywhere still extremely primitive, and so far as we can now see, ordinary milk, in a fresh state, will indefinitely remain a most dangerous food, the disadvantages of which, in respect to the general supply, can only be obviated by the proper application of pasteurization. This process is now obligatory in some of our large cities for all grades of milk except certified and inspected, and is also quite widely used in the milk trade even where not compulsory, but commercial pasteurization should be considered adequate only when carried out under conditions which assure a fresh and not excessively contaminated supply, heated to the requisite temperature of 60 C. for a period of twenty minutes, quickly cooled and kept iced, delivered early and consumed without delay, for such milk is prone to rapid fermentative changes. It is clear that these conditions can be enforced only by a system of strict and energetic official control, which is as yet impossible of realization in most communities. As at present carried on, pasteurization of market supplies is often worse than useless, because of the inadequacy of the methods used, and the insufficiency of the system of supervision by proper authority; and I am therefore very strongly of the opinion that while we should be unremitting in our advocacy of all possible improvements in dairy hygiene, including compulsory efficient pasteurization, we should, however, for the present teach that the only absolutely safe milk is that which is heated within the home of the consumer. Milk which is brought to just below the boiling-point in the family kitchen will never transmit bovine tuberculosis to the babies of the household; and since we are no longer afraid of the bogey of destroyed "vital principles" or what not in heated milk, knowing that the only "vital principles" in milk when it reaches the consumer are such as are contained in the bodies

of the living and oft-times pathogenic bacteria with which it is contaminated, I am coming more and more to believe that, for infant-feeding, at least, all grades of milk should be so treated. It is, at any rate, imperative that young children should be given raw milk only when known to have been derived from cattle free from tuberculosis.

It is unquestionably our duty as physicians to instruct our patients and the public that bovine tuberculosis is, without giving it undue weight and always keeping it in proper subordination to the larger problem of infection from human sources, a grave menace to human health, but that it is, by the simple expedient of home pasteurization, a disease most easily prevented in man; and as typhoid fever is now coming to be regarded as a reproach to the community in which it occurs, so must this disease become.

Berkeley National Bank Building.

THE INFLUENCE OF LACTOSE ON THE METABOLISM OF AN INFANT

WITH SPECIAL REFERENCE TO FAT, NITROGEN AND ASH *

FRITZ B. TALBOT, M.D. AND LEWIS W. HILL, M.D.

BOSTON

As there are very few metabolism experiments which throw much light on the digestion of sugar and its effect on the digestion and absorption of the other food components, the following investigation was undertaken to increase our knowledge of this phase of the subject.

J. P. entered the Massachusetts General Hospital, Sept. 12, 1913, at the age of 5 months. The family history was negative. The baby was born prematurely at seven months, April 11, 1913, weighing $4\frac{1}{2}$ pounds, (2.05 kg.). He was never breast-fed and had been given condensed milk or modified milk with proprietary foods containing maltose and had never thrived. During July he had "cholera infantum." He entered the Boston Floating Hospital, Aug. 14, 1913, where he remained until he was transferred to the Massachusetts General Hospital, one month later (Sept. 12, 1913), at which time he weighed 9 pounds 15 ounces (4.54 kg.).

The physical examination showed that the child was moderately emaciated, very much under weight, but there was no evidence of rickets. The examination was otherwise normal. The digestion was weak. The von Pirquet skin test was negative. During the patient's stay in the hospital his progress was as follows:

Sept. 19: He was moderately emaciated; color pale, but he was playful and smiled. His food at this time was: Fat 2.00, lactose 5.63, protein 1.63; 1,400 c.c. in twenty-four hours.

September 25: The amount of sugar was increased and he received: fat 1.95, lactose 7.32, protein 1.71; 1,400 c.c. The only abnormal factor recorded at this time was a diffuse subcuticular redness of the face on the 28th, which lasted only twenty-four hours.

October 2: The food was: fat 1.66, lactose 9.93, protein 1.78; 1,400 c.c. There was very rapid gain in weight, strength and general condition. The flesh became firmer; there was no edema. There was no irritation from the stools.

Oct. 8: Fat 1.75, Lactose 14.0, protein 1.80; 1,400 c.c. This was taken well for forty-eight hours; then he refused part of his food, regurgitated a portion and began to have frequent loose, green, acid stools, which irritated the buttocks and made them red. He was uncomfortable. The lactose in the food was, therefore, diminished, October 10, so that he received fat 1.55, lactose 9.15, protein 1.71. After this he took the food better but continued to have some discomfort and six large, watery, green stools a day, containing many small soft curds and a few large tough curds, with a moderate amount of mucus. The physical examination, including the ears, showed no extraneous cause for the symptoms of indigestion.

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

* From the Children's Medical Department, Massachusetts General Hospital.

October 14: The formula was: fat 1.67, lactose 4.60, protein 1.84; 1,400 c.c., which corresponded closely with the amounts given in Period 1. He immediately became comfortable, regained his appetite and only passed one formed, hard, yellow stool a day. After this the formulas were:

October 23: Fat 2.60, lactose 4.47, protein 1.70; 1,400 c.c.

October 30: Fat 3.14, lactose 4.38, protein 1.75; 1,400 c.c.

(For weight, calculated calories and temperature, see chart).

METHOD OF PROCEDURE

A sample of the food was taken each day during the metabolism periods and examined. The baby was made comfortable on a Bradford frame devised by one of us and previously described.¹ Each period was marked off with charcoal. All the periods commenced at noon, after which time all the urine was collected and saved until noon three days later. (Thymol was used as a preservative.) It was assumed that this urine was representative of the metabolism, since the same amount and percentage of food was given to the baby for at least two days in one instance, and for three days in all others before the period was commenced. Charcoal was placed in the noon feeding at the beginning of the period and in the noon period at the end of the period to mark off the stools. All the stools were collected from the first appearance of the charcoal, until the next stool containing charcoal appeared three days later. The first charcoal stool represented the beginning of the period and was saved, and the second charcoal stool represented the end of the period and was thrown away.

The amounts of food taken were carefully measured and any food that was not taken was subtracted from the daily intake.

The chemistry was done by one of us (Hill) in the Department of Biological Chemistry at the Harvard Medical School.

Methods.—The total nitrogen of the milk, urine and feces was determined in the usual manner by the Kjeldahl method. The figures representing protein were found by multiplying the nitrogen by the factor 6.37.

Fat.—The milk-fat was determined by the Adams paper coil which was extracted in a Soxhlet apparatus.² The fat in the stool was determined by the Folin-Wentworth method.³

Sugar.—Milk-sugar was determined by titration with Fehling's solution. Although this is not a particularly satisfactory method because the end point of titration is not abrupt, it is simple to perform

1. Talbot, F. B.: Apparatus for Metabolism Experiments in Male Infants, Jour. Am. Med. Assn., Nov. 27, 1909, p. 1818.

2. Hawk: Physiological Chemistry.

3. Folin and Wentworth: Jour. Biol. Chem., 1910, vii, 421.

and sufficiently accurate for the purpose of this investigation.⁴ Qualitative tests were made for sugar in the stool.⁵

Ash.—A silica crucible was used in the determination of the ash. Great care was taken during incineration not to use too much heat, to prevent the loss of the chlorids of milk, which are volatile at high temperatures.

TABLE 1.—

Percentage Composition of Food	Food				Feces						Acidity of Feces
	Fat, gm.	Protein N., gm.	Sugar, gm.	Ash	Total Fat	Soaps and Fat Acid	Neut. Fat	N.	Sugar	Ash	
1											
F. 2.00	75.97	64.98 (N = 10.20)	216.72	19.58	8.38	7.45	0.93	1.15	0.00	5.74	36.6
C. 5.63											
P. 1.63											
2											
F. 1.95	81.90	72.23 (N = 11.34)	307.44	18.90	7.67	6.93	0.74	0.67	0.00	5.17	33.9
C. 7.32											
P. 1.71											
3											
F. 1.66	69.72	74.91 (N = 11.76)	417.06	16.86	6.92	5.78	1.14	1.11	0.00	5.30	54.9
C. 9.93											
P. 1.78											
4											
F. 1.53	57.87	63.15 (N = 9.90)	336.12	12.75	14.46	8.46	6.00	2.01	0.00	7.17	255.0
C. 9.16											
P. 1.71											
5											
F. 1.67	70.14	77.58 (N = 12.18)	193.20	17.85	4.43	3.71	0.72	0.96	0.00	4.98	13.13
C. 4.60											
P. 1.84											
6											
F. 2.00	84.00	71.66 (N = 10.35)	187.74	14.71	6.43	5.78	0.65	0.86	0.00	5.79	6.58 Alk.
C. 4.47											
P. 1.70											
7											
F. 3.14	130.93	73.25 (N = 11.50)	182.64	16.68	9.71	8.37	1.34	0.83	0.00	5.46	12.38
C. 4.38											
P. 1.75											

Acidity of the Stools.—It was found impractical for various reasons to determine the acidity of the fresh moist stool. This would have been the ideal procedure. All the determinations of acidity were made on the dry stool, although we realize that these figures are not

4. The Wollny refraction meter was tried but found unsatisfactory and discarded.

5. Tests were made with Benedict's, Fehling's and Nylander's reagents as well as with phenylhydrazin.

of *absolute* value because some of the lower fatty acids may volatilize during the drying, they are of great *relative* value in comparing the acidity of the stools in different periods. One gm. of dried feces was weighed out, rubbed up in a mortar with a little water to the consistency of a thin paste, and then transferred to a beaker, enough water being added to make it up to about 100 c.c. This mixture was then

—METABOLISM OF J. P.

Urine		Absorbed			Retention		Body Weight			Cal. per Kilo per 24 ^h	No. of Stools in Period
Total N.	Ash	Fat Per Cent.	N., Per Cent.	Ash Per Cent.	N	Ash	Start of Period	End of Period	Gain or Loss		
6.99	7.26	88.90	88.90	71.52	+2.06	+6.58	4,400	4,450	+ 50	133	5
8.40	7.35	90.64	94.10	72.70	+2.27	+6.38	4,535	4,850	+315	171	6
7.49	6.80	90.08	90.54	68.50	+3.16	+4.76	4,975	5,250	+275	181	3
6.06	6.45	74.99	79.58	43.59	+1.80	— .60	5,300	5,115	—185	135	12
11.27	9.58	93.69	92.20	72.11	— .05	+3.29	5,125	5,000	—125	115	3
10.35	5.59	92.35	92.33	60.62	+ .04	+3.38	5,050	5,150	+100	123	6
9.26	7.66	92.59	92.76	67.11	+1.41	+3.56	5,275	5,450	+175	141	4

brought to a boiling-point and kept just below this for fifteen minutes, being shaken every minute or two. It was then filtered, washed out with hot water and the acidity of the filtrate was determined by titrating with fiftieth-normal sodium hydroxid with phenolphthalein as the indicator.

Results.—Table 1 gives the results of seven periods. Table 2 gives the percentage composition of the dried stools with a description of the character of the stools passed during each period.

DISCUSSION OF RESULTS

Clinical.—During Period 1, while the baby received 133 calories per kilogram of body weight there was slight gain in weight; in Period 2, with 7.3 per cent. lactose and 171 calories per kilogram of body weight, there was a very rapid gain of 315 gm. in three days. Clinically, this gain did not seem to be due to retention of fluid (there was no edema), but to the actual formation of new fat. A gain of 275 gm. continued in Period 3, when 181 calories were taken. The digestion in all three periods was apparently perfect. Four days before Period 4 was commenced a larger percentage of sugar was given, but as there were loose watery, acid, burning stools on the following day, the percentage of sugar was reduced to the same percentage as in Period 3, when there had been no symptoms of indigestion. During Period 4 the stools were irritating and contained both fat curds and casein curds.

A glance at Table 1 will show how well the figures representing the per centage of fat and nitrogen absorbed, correspond with the clinical records showing an excess of soft, fatty curds and hard casein curds in the stools. The sugar was again reduced, so that in Period 5 there was one firm stool a day. During Periods 4 and 5 there was a loss in weight. The amount of fat was therefore increased in Periods 6 and 7 and he began to gain weight rapidly.

The Metabolism of Lactose.—Sugar was not found in either the urine or the stools in any of the seven periods, and we feel that none was lost in the form of sugar from the body. The acidity of the stools remained about the same in Periods 1 and 2, and increased slightly in Period 3. In Period 4 there was a sudden increase in acidity to five times as much as in the previous period, and coincidently the characteristic green watery, acid stools appeared. Escherich was the first to draw attention to this type of stool as a symptom of fermentation of sugar, and our experience coincides with his teachings. These stools gave qualitative tests for lactic, acetic, succinic and butyric acids.⁶ It is conceivable that such bacteria as the *Bacillus lactis aerogenes*, the *Bacillus bifidus*, the *Bacillus acidophilus* and the colon group, can be fed so much sugar that their activity increases to such an extent that they carry the catabolism of sugar beyond the usual point. This becomes fermentation of sugar when it goes beyond a certain point, the end-result being the acids enumerated above. When these acids are present in large enough amounts, they become irritants and the body proceeds to rid itself of them in the quickest manner. Any irri-

6. Succinic acid was found by the pyrrol test; lactic by the Uffelmann and also Hopkins and Cole tests; acetic by sulphuric acid plus alcohol, which resulted in the characteristic odor; butyric sulphuric acid and odor. These acids had previously been separated so far as possible by fractional distillation.

TABLE 2.—PERCENTAGE COMPOSITION OF DRIED STOOLS

Period	Percentage Composition of Dried Stool						Number of Stools	Character of Fresh Stool
	Weight of Dried Stool	Soaps and Fat Ac. Pct.	Neut. Fat Per Cent.	Prot. Pct.	Ash Pct.	Total Pct.	Other Substances Per Cent.	
1	27.76	26.89	3.3	26.3	20.6	77.2	22.8	Large, formed, hard, light yellow. Large, formed, hard, light yellow. Formed, but much softer than before. Very large. One green stool, the rest light yellow. Large, watery, green with many small soft curds and a few large hard curds. Moderate amount mucus. Large, formed, hard, light yellow. Small, very hard, scybalous. Light yellow. Small, hard, light yellow.
2	24.93	27.8	3.0	20.7	20.7	72.2	27.8	
3	26.15	22.1	4.3	27.5	20.3	74.2	25.8	
4	44.55	19.0	13.5	29.0	16.0	77.5	22.5	12
5	21.88	17.0	3.2	29.0	22.0	71.0	29.0	3
6	25.33	22.8	2.5	21.6	22.8	69.7	30.3	
7	26.92	31.11	4.98	19.7	20.3	74.0	26.0	4

tating substance in contact with the intestinal mucous membrane stimulates the formation of mucus and causes increased peristalsis. This causes the food to be moved along more rapidly than usual and there results an increased number of stools. The fat and casein may be carried along so rapidly that their digestion is not completed and they may appear in the form of fat and casein curds. In period 4 the percentage of fat absorbed dropped from about 90 per cent. (Period 3) to 74.99 per cent., and the absorption of nitrogen decreased from 90 per cent. to 79.59 per cent. The absorption of both of these elements of the food returned to over 92 per cent. in the subsequent periods, when the stools were normal in number and character.

Lactose and the Retention of Nitrogen.—The increasing amounts of lactose was accompanied by greater retention of nitrogen. In Period 3 it reached 3.16 gm. in the three days. A possible explanation of this fact may be found in the work of Kendall and Farmer⁷ on the metabolism of bacteria, which goes to show in the test-tube that, when sugar was present in the food, less ammonia nitrogen was formed than when sugar is absent. If the results found in the test-tube are applicable to the intestinal canal, it seems probable that the reason more nitrogen is retained in the body when sugar is present is not that the sugar makes the nitrogen more easily absorbed, but that the intestinal bacteria use the sugar in preference to the protein and form less nitrogen to be carried away in the stools, or in other words, they leave a larger amount for absorption in the body. In Period 4 the nitrogen retention was lowered to one-half of that in the previous period. In the next two periods (5 and 6) there was essentially a nitrogen equilibrium. The figures shown in Periods 1, 2 and 3 correspond with those given by Keller, Rothberg, Massaneck, Rommel, Tada and Orgler,⁸ who found that the sugar in the food influenced the retention of nitrogen in the body.

Lactose and the Digestion and Absorption of Fat.—The literature of the physiology and pathology of the metabolism of fat has been summarized by Freund⁹ and by one of us,¹⁰ so that it will not be given again in this article.

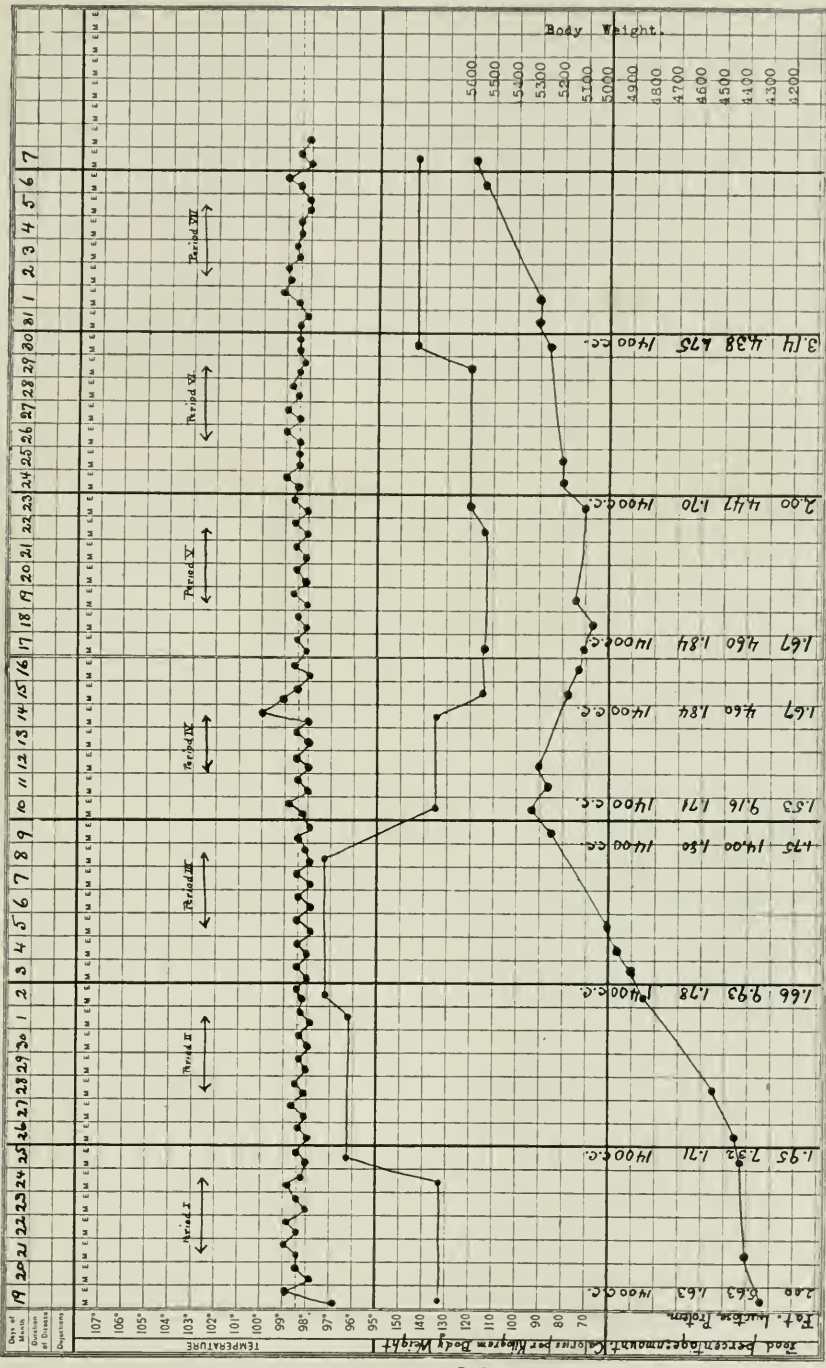
Table 2 shows that increasing amounts of sugar did not influence the splitting of fat so long as the digestion remained normal. The percentage of fat that was split was very high in Periods 1, 2 and 3,

7. Kendall and Farmer: Jour. Biol. Chem., 1912, xii, Nos. 1, 2 and 3; xiii, No. 1; 1913, xv, No. 2.

8. Orgler: Der Eiweisstoffwechsel des Sauglings; Ergebn. d. inn. Med. u. Kinderh., 1908, ii, 486.

9. Freund: Ergebn. d. inn. Med. u. Kinderh., 1909, iii, 139.

10. Talbot: AM. JOUR. DIS. CHILD., 1911, i, 173-192.



Road Percentages: Fat, Lucine, Protein, Body Weight
 Temperature: 107° to 100°
 Date of Experiment: 1920.21 to 30.31

being respectively 89 per cent., 91 per cent. and 84 per cent. In Period 4 only 60 per cent. was split when there was diarrhea.

The absorption of fat remained high in all periods except Period 4, when there was an acid diarrhea and about 25 per cent. of the fat in the food was lost in the stools. (This loss of fat plus the loss of protein added up to 186.7 calories in two days, which represents 15 calories of food per kilogram of body weight that were not absorbed at all. The high acidity of the stool represented sugar that was not utilized and may be considered as evidence of a further loss of energy.)

The Acidity of the Stool.—The methods of determining the acidity of the stool in this investigation were very crude, and, as was stated above, we consider that the figures are only of relative value. The acidity of the stool in cubic centimeters of tenth-normal sodium hydroxid increased fivefold from Period 3 to Period 4.

Although no definite conclusions may be drawn from these figures, a very suggestive explanation may be given for the diminished absorption of fat while the stools were acid. Either the irritating acids increased the intestinal peristalsis so much that the food was not in the intestinal canal long enough for complete splitting and absorption of the fat, or the acidity was so great that the bile acids were decomposed and the emulsion of fat interfered with in such a manner that it could not be absorbed in the usual manner.¹¹ It is possible that both of these factors played a part in the diminished absorption of fat during this period.

Lactose and the Retention of Ash.—With each increase in the amount of sugar beyond 7 per cent., there was less ash retained in the body, while in Period 4 more ash was excreted than was ingested (there was a negative balance). During the subsequent periods with the sugar and protein in the food stationary and with increasing amounts of fat, the ash balance for all three periods was positive and essentially the same. These figures seem to indicate that the sugar plays a very important part in the retention of ash, and possibly a greater part than either fat or protein. It is necessary to discuss in this connection the question whether most of this ash represents calcium and magnesium, or sodium and potassium. It was impossible to include these estimations in this investigation.

Calories.—This investigation might be criticized in that varying amounts of food energy were given in the different periods and that, as a result, the infant was overfed in some periods and underfed in others. In another publication,¹² which is shortly to appear in conjunc-

11. See Moore and Krumbholz: Jour. Physiol., 1897-98, xxii, p. liv.

12. Carnegie Inst. Wash., Pub. 201, Washington, 1914; AM. JOUR. DIS. CHILD., 1914, viii, 1.

tion with Dr. F. G. Benedict, one of us (F. B. T.) has figures to show which indicate that the traditional number of 120 calories per kilogram of body weight do not apply to all babies; that the basal metabolism of an atrophic baby may be 100 per cent. greater than that of a healthy, well-nourished, fat, normal infant. For this reason we believe that discussion of this point must be deferred until further data are available on the subject.

CONCLUSIONS

1. Increasing amounts of sugar up to a certain limit increase the retention of nitrogen, and beyond that point may diminish the absorption and possibly the retention of nitrogen.

2. Increasing amounts of sugar do not affect the absorption of fat up to a certain point, beyond which point there may be a diminished absorption of fat.

3. Sugar given beyond certain limits may result in a greatly increased acidity of the stool and diarrhea. The diarrhea is probably a result of the increased peristalsis. Clinical evidence of a carbohydrate fermentation is the scalded, irritated skin of the buttocks and the green, watery acid stools.

4. The retention of ash seems to depend on the amount of sugar in the food. When the amount of sugar is increased beyond a certain point, there may be a negative balance and the ash may be lost from the body. It is impossible to say whether this negative balance is due to the diarrhea, or the increased acidity of the stool, or other factors in which fat plays a part.

5. Clinically, the amount of sugar which an infant can digest and absorb varies with the individual. There is no fixed point in a given individual at which sugar will or will not be digested at a given time. Other factors than the amount of sugar may influence its digestion.

311 Beacon Street—23 St. John Street.

EXAMINATION OF THE CHEST IN CHILDREN *

RICHARD M. SMITH M.D., AND CLIFFORD D. SWEET, M.D.

BOSTON

FRESNO, CAL.

The importance of the examination of the chest in children was forced on our attention in the Children's Department at the Massachusetts General Hospital because of the large number of patients brought to us by school nurses and friendly visitors to determine whether or not tuberculosis was present. It has been our custom in doubtful cases in addition to the customary physical examination to do a von Pirquet skin reaction and to have a roentgenogram made of the chest. We have recorded also the weights and tried to secure the morning and evening temperature. The same methods of examination have been employed in other patients having symptoms pointing to disease of the lungs. We have tabulated the results of our studies in 100 cases (all of these patients have been examined by one of us, and nearly all of them by both of us). The course of events has been followed for many months in most of the children so that our diagnoses have been proved. A few cases have been seen for the first time within a few weeks. The primary interest in this connection is and will remain, of course, in determining the presence or absence of tuberculosis, but if we are content to leave the matter there many important conditions will be overlooked. It is essential also to bear in mind the distinction between tuberculous infection and active tuberculous disease. The prevalence of healed tuberculous lesions found on post-mortem examination is too well known to need discussion. Tuberculous infection can be determined ante mortem in most instances, but this does not mean that the individual so infected has active tuberculous disease and needs to undergo treatment. If treatment were indicated in all such infected individuals, most of us would be in sanatoriums. After the presence of tuberculous infection has been determined it is necessary to decide whether or not that infection is active. Many non-tuberculous patients will show infection with some other organism and may require active treatment.

CLINICAL DATA

Age.—The ages of our patients varied from 1½ to 13 years. The majority were from 5 to 10 years.

* From the Children's Medical Department Massachusetts General Hospital.

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

Temperature.—The temperature records were taken in the clinic and at home either by a district or hospital nurse, and in some instances by mothers. In all but 23 out of the 100 children the temperature was as high as 99 on at least one observation, and in only 14 instances did the temperature go above 99.8. In these 14 cases the maximum temperature was 100 in 10, and 100.2, 100.6, 101 and 102 in the others. These highest temperatures, except in one instance, were due to other causes than tuberculosis. Eight of the 14 cases with elevated temperature had no tuberculous infection; 3 had active tuberculosis. In the whole series of 100 cases there were 9 children with active tuberculosis, and only 3 of these showed at any time a temperature above 99.4. From these observations it would seem that slight rises in temperature are common, and when present, even in patients showing lung symptoms, are more often due to some other cause than tuberculosis, and that tuberculosis may be present with very little or no elevation in temperature.

Weight.—The weights of patients were taken in the clinic and compared with the average weight of children of the same age. Sixty-five children were underweight. Two of the patients with active tuberculosis were above the average weight. This factor by itself is of relatively little importance, because it is largely dependent on food and general hygiene.

Night Sweats.—Only ten cases in the whole series had night sweats. None of these ten cases had active tuberculosis. Stating this in another way, none of the cases of active tuberculosis had night sweats. This bears out the common impression that in children this sign is of no assistance in the differentiation of tuberculosis from other infections.

Cough.—Cough in this series is of no value as a comparative factor since all the patients had this symptom except those brought to the clinic for examination of the lungs because of known exposure to tuberculosis.

General Malaise.—Under this symptom may be included all the complaints which describe the feeling of being ill. The presence of this symptom may of course be due to disease from any organism, but it is not safe to conclude that its absence excludes tuberculosis. Four of our patients with active tuberculous disease appeared to be in perfect health. The diagnoses in these patients were made only because of the routine examination.

Exposure to Tuberculosis.—Thirty-four children gave a history of known exposure to tuberculosis. Of this number only 6 had a negative von Pirquet reaction. These 6 have all been followed. No further signs of tuberculosis have developed and their general condition has improved. There seems to be no good reason to doubt the accuracy

of the reaction. In 2 cases the positive von Pirquet was the only sign of tuberculous infection. Of the 34 cases with known exposure, 18 showed on examination signs in the lungs, 22 had a positive D'Espine's sign and 30 showed by roentgenoscopy some pulmonary lesions; only 5 had active tuberculosis, 3 of the lungs, 1 of the bones and 1 of the eye. It would seem from this study that only a very small proportion of children who are exposed to tuberculosis escape infection, but that a considerable number of those infected are able to survive the active stage of the disease.

Sputum.—It is harder to secure sputum in children than in adults, but if obtained it is of the same value. Only 4 of our cases with active tuberculosis had a sputum examination, and 2 of these were positive for tubercle bacilli. Twenty-five cases out of the whole series had a sputum examination, most of them repeatedly. Five showed influenza bacilli in sufficient proportion, so that the diagnosis of influenza bronchiectasis was made. This condition is of course as definite an entity as tuberculosis and deserving as careful study. Eighteen cases showed in the sputum so many organisms that no single one could be considered of etiologic significance.

COMPARISON OF LUNG SIGNS AND THE ROENTGEN RAY

The physical examination of the lungs was negative in 34 cases. No roentgenogram was taken in 2 of these, in 4 roentgenoscopy was negative, in 20 it showed only an enlargement of the glands or thickening about the lung roots, in 4 it showed slight haziness at one apex, in 3 a process in the midst of a lobe and one was a patient with pertussis. Sixty-six cases on examination showed signs in the lungs—dulness, changes in breathing, increased fremitus or the presence of râles. The Roentgen findings coincided with the clinical examination in 49 cases, or 74.24 per cent. In the other 17 patients the examination of the lungs showed in 14 cases slight dulness at one or the other apex, and in 3 cases a few scattered râles, but the roentgenogram was clear. These figures show a remarkable agreement between the physical examination of the chest with negative or positive findings and the roentgenograms.

If we approach the subject from the other angle, 89 cases showed by roentgenoscopy some lesion in the chest. This might seem an unduly large number, but it must be remembered that all the 100 cases under study were selected because of symptoms which would indicate some pathologic condition in the chest.

Disregarding for the moment the question of bronchial glands, there were 52 instances in which roentgenoscopy revealed some lesion in the lungs themselves; of these, 41 cases, or 78.84 per cent., showed

signs in the lungs by the ordinary methods of auscultation and percussion; 11 cases, or 21.15 per cent., did not show anything on physical examination. The Roentgen ray in 7 of these negative cases showed only slight haziness at one apex, and in the other 4 a process in the midst of the lung.

In no patient without symptoms in which the Roentgen ray alone showed a departure from the normal was there considered to be sufficient evidence for active treatment. The Roentgen ray did serve in two patients with symptoms to make us surer than we could have been otherwise that the trouble was in the lungs. It would seem that as an aid to clinical examination of the lungs, especially in the study of deep-seated lesions, the Roentgen ray is valuable, but it is not to be taken as a method to replace a careful physical examination of the chest.

BRONCHIAL GLANDS

The signs usually considered in the diagnosis of enlarged bronchial glands are increased dulness with change in the breath-sounds and fremitus along the sides of the vertebral column at the level of the scapulae; transmission of the nasal quality in the whispered voice as heard over the vertebrae below the first dorsal, and roentgenograms. Certain other signs, such as dilatation of the superficial veins of the front of the chest and dulness over the manubrium, occur in exceptional instances. Other rare signs are due to pressure on the laryngeal nerves. One of our patients had only one complaint, hoarseness, coming on gradually, but well marked when first seen. He showed paravertebral dulness, D'Espine's sign and a positive roentgenogram. The von Pirquet reaction was negative and there was no other indication that he had a tuberculous infection. Under observation his hoarseness has gradually improved and coincident with this the D'Espine sign has decreased from the fifth to the third dorsal vertebra, and the roentgenogram has shown the shrinking of the glands. In the 100 cases, 20 showed dulness with or without change in breathing at the lung roots and in every instance the D'Espine sign was positive and the Roentgen ray revealed bronchial glands or thickening of the lung roots except in 2 cases in which the D'Espine sign was not recorded, but the roentgenogram was positive. Seventy out of the 100 cases had a positive D'Espine sign down to or below the second dorsal vertebra. Of these, 65, or 92.85 per cent., had positive roentgenograms, 3 had negative roentgenograms and in 2 no roentgenograms were taken. Two of the cases in which roentgenoscopy was negative showed D'Espine's sign to the fifth, the other to the second dorsal vertebra. There is no explanation for these discrepancies, but it would seem, except in rare instances, that a positive D'Espine sign means enlarged

bronchial glands. The only case which we were able to follow to post-mortem examination showed paravertebral dulness, a positive D'Espine and a positive roentgenogram, and at necropsy there was marked enlargement of the bronchial glands. In 16 instances the roentgenogram was the only evidence of enlarged bronchial glands, and the plate often showed in these instances a marked enlargement. Presumably these glands were so situated as to cause no pressure and thus escaped detection. The 70 cases with positive D'Espine's sign shown a positive von Pirquet reaction in 41 instances, or 58.57 per cent., a negative reaction in 27, or 38.57 per cent., and in 2 the test was not done. The one instance of enlarged bronchial glands examined post mortem had a negative von Pirquet, and no tuberculous focus was found at necropsy. The glands in this case were due to an acute endocarditis. These figures emphasize the importance of remembering that a diagnosis of enlarged bronchial glands does not mean necessarily tuberculous glands. In several instances it was possible to observe by the D'Espine sign and the Roentgen ray the appearance and disappearance of the bronchial glands during the course of an acute bronchitis or endocarditis. Any infection in any part of the body drained by these glands may give rise to their enlargement.

VON PIRQUET REACTION

There were 62 positive and 35 negative von Pirquet reactions, and in 3 patients the test was not done. Of the 62 positive cases, 24, or 38.7 per cent., had a known exposure to tuberculosis, 45 had a positive D'Espine sign and 56 showed signs in the lungs by Roentgen examination. Only 7 of the positive reactions were in patients having an active tuberculosis; the others had without doubt a healed process in many instances shown by some physical sign. None of the cases with negative reaction had tuberculosis proved by other means, but many of them showed physical signs of disease in the lungs.

CASE 1 (5).—This patient was 11 years old and came to us complaining of a cough which had lasted for several years. It was especially severe during the winter and accompanied by a considerable amount of sputum. The examination of the lungs was negative except for a few scattered râles. Repeated examinations of the sputum showed no tubercle bacilli. D'Espine's sign was negative. Roentgenoscopy revealed the lung markings matted together and abnormally dense especially on the right, more marked at the base; the apices normal. The von Pirquet reaction was negative. This case was considered to be one of chronic bronchitis.

CASE 2 (11).—This patient, 12 years old, complained of cough lasting for several months with profuse expectoration. The examination of the lungs showed many small areas of dulness over both bases without change in breathing and many scattered coarse râles. Repeated examinations of the sputum showed no tubercle or influenza bacilli. The D'Espine sign was negative. Roentgenoscopy revealed enlarged glands at both roots, especially the right, with slight thickening of the linear markings, right apex slightly dull. A sec-

and roentgenogram several months later showed some pathologic process at the root of the right lung. Fluoroscopic examination showed that the diaphragm on the left did not move so well as on the right, and that there was a dull spot at the root of the right lung. Several von Pirquet reactions were done and were negative. This patient had been at a state sanatorium for tuberculosis and the case was recorded in the classification of that institution as "not determined." It was considered by us to be one of chronic infection of the lung roots with some organism not the tubercle bacillus.

CASE 3 (39).—A child of 5 years, who three years ago had pneumonia, since when about every two months, she had had attacks of coughing lasting from two to three days accompanied by pain in the side, fever and profuse yellow expectoration. The cough did not entirely disappear between attacks. On examination the lungs showed increased paravertebral dullness and slightly impaired resonance over the right base. The sputum showed no tubercle bacilli and no influenza bacilli, but many other organisms. D'Espine's sign was positive to the fifth thoracic vertebra. The Roentgen ray showed enlarged bronchial glands and a pathologic process involving both lungs. The von Pirquet reaction was negative. This was considered to be a case of chronic bronchitis, quite possibly bronchiectasis.

CASE 4 (53).—A child, 4 years old, who complained of attacks of coughing coming once or twice a month lasting two or three days and accompanied by fever and thick yellow sputum. On examination the lungs showed dullness with distant breathing and moist râles at the right base. D'Espine's sign was positive to the fourth thoracic vertebra. The Roentgen ray showed enlarged bronchial glands and some pathologic process at the root of the right lung with a dull area in the region of the right bronchus. The von Pirquet reaction was negative. It is fair to say that the Roentgen interpretation said "bronchiectasis or bronchopneumonia, no evidence of tuberculosis." It was considered to be a case of bronchiectasis.

CASE 5 (65).—A child, 10 years old, who came to us with the statement that three years ago she had had pneumonia and since then she had caught cold easily. She had attacks of fever and recently a considerable amount of sputum. She had had no night sweats. Examination of the lungs showed slight dullness at the right apex without change in breathing except during the time when she had a cold; then there were a few scattered râles. Repeated examinations of the sputum failed to show any tubercle bacilli or influenza bacilli. D'Espine's sign was positive to the fifth thoracic vertebra. The Roentgen ray revealed enlarged bronchial glands and a pathologic process involving both lungs. Repeated von Pirquet reactions were negative. This was believed to be a case of bronchiectasis.

CASE 6 (66).—A child, 10 years old, who for two months had had pain in the back and recently had begun to have a considerable amount of thick yellow sputum. On examination the lungs showed at the right apex dullness without other changes and dullness in the middle of the left lung and toward the left base with slight change in breathing and medium and fine crepitant râles. Many examinations of the sputum showed no tubercle bacilli or influenza bacilli. D'Espine's sign was positive to the fourth thoracic vertebra. Roentgenoscopy revealed enlarged bronchial glands and mottling of both lungs, more marked about the roots but extending to the apices. The von Pirquet reactions were negative. This was considered to be a case of bronchiectasis.

The analysis of these cases has shown that only 9 out of 100 suspected cases had active tuberculosis; that 63 had evidence of tuberculous infection, now in a quiescent state, and that 39 had no evidence of tuberculosis of any kind. It is important to find the cases of active tuberculosis and give them the proper care. It is equally important to

be sure that this diagnosis is correct. Patients with old inactive scars of tuberculous infection should not be treated as cases of active tuberculosis. A considerable number of children suspected of having tuberculosis will be proved to have an infection with some other organism than the tubercle bacillus. These patients need proper treatment. A part of this treatment consists in keeping them away from exposure to tuberculosis either outside or in a tuberculosis sanatorium. These patients deserve and should receive the most careful consideration.

329 Beacon Street.—Griffith-McKenzie Building.

THE ABSORPTION OF FAT FROM THE INTESTINAL TRACT OF THE ACTIVELY TUBERCULOUS CHILD *

FREDERIC W. SCHLUTZ, A.B., M.D.

Assistant Professor of Pediatrics, University of Minnesota.

MINNEAPOLIS

The question of fat absorption from the intestinal tract of the actively tuberculous child is one of considerable importance. This is particularly true in view of the fact that it is almost a universal custom to feed the tuberculous child on a diet especially rich in fat.

Two things are considered advantageous to the tuberculous child: (1) to bring about as rapidly as possible a pronounced increase in weight; (2) to have this gain represented as much as possible by the deposit of fat in the tissues. While both of these considerations were purely empirical, the extensive studies on food metabolism carried out in recent years have shed much light on the factors which should influence the choice of diet for this affection.

It has been shown that diet may not only affect the chemistry of the tissues of an organism to a very marked degree but also play an important rôle in influencing the resistance of the tissue to disease process.

Weigert¹ has shown by experiments on animals that both the fat metabolism and the water metabolism of the tissues are important factors. He has shown that the age of the animal and the manner of feeding determine the water retention. The amount of water content in the tissue depends not only on an increase or decrease of fat substance in the tissue but also on variations of the fat-free residual substance in them.

The tissues of the animal fed on protein and fat-rich food show the largest amount of fat-free residual substance and are low in water content, while conversely those fed on food low in protein and fat, but rich in carbohydrate, show a small per cent. of fat-free residual content but retain much fluid. He has further demonstrated by experiments on pigs infected with tuberculosis that animals fed on

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* From the Minneapolis City Hospital and the Department of Medicine of the University of Minnesota.

1. Weigert, R.: Ueber dem Einfluss der Ernährung auf die chemische Zusammensetzung des Organismus, *Jahrb. f. Kinderh.*, 1905, lxi, 178; Ueber dem Einfluss der Ernährung auf die Tuberkulose, *Berl. klin. Wchnschr.*, 1907, xliv, 1209.

carbohydrates and with pronounced water retention in their tissues are the least resistant to this infection, whereas those fed on fat-rich mixtures, resulting in low water retention and high specific gravity of the tissues, succumbed much less readily to the inroads of this disease. Fattening the animals rapidly by forced feeding did not seem to hinder in any particular way the destructive influence of the infection. Weigert's experiments seem to emphasize the important relationship of fat metabolism and water retention of the tissues to the production of immunity.

The importance of diet in its relationship to tissue metabolism is further emphasized by Czerny's² important studies and publications on the exudative diathesis or the scrofulous manifestations of the older writers. He calls attention to the extremely intimate connection existing between these manifestations and the diet. This is shown by the reaction of individuals affected with the exudative diathesis to certain kinds of food. With few exceptions, such as are cited by Finkelstein,³ overfeeding or attempts to bring about forced gain in weight results in the prompt appearance of these manifestations or in their aggravation, if already present. The reaction seems particularly prompt and pronounced if milk, cream, eggs or large quantities of concentrated sugars form the chief ingredients of the diet.

There is still much difference of opinion whether many of the scrofulous or exudative manifestations are tuberculous in their nature or not. This fact has been clearly shown, that the selection of a diet which is not especially rich in fat and which does not favor retention of fluid in the tissues influences favorably the scrofulous or exudative manifestations in the tuberculous child.

Just what particular part of the metabolism of the scrofulous or exudative child is abnormal is not definitely known. Both fat and salt metabolism have been suspected. That the fat absorption in children with this condition differs very little from the normal was shown by experiments of Birk⁴ and L. F. Meyer.⁵

The importance of the fat metabolism for the tuberculous child brings up the question of the fat absorption from its intestinal tract.

2. Czerny, A.: Die exudative Diathese, *Jahrb. f. Kinderh.*, 1905, lxi, 199; Exudative Diathese Skrofulose und Tuberkulose, *Jahrb. f. Kinderh.*, 1909, lxx, 529; Erfahrungen über den Verlauf der Tuberkulose im Kindesalter, *Arch. f. Kinderh.*, 1913, lx, 242; Zur Kenntnis der exudativen Diathese, *Monatschr. f. Kinderh.*, 1907, vi, 1; Ueber die Beziehung zwischen Mästung und scrofulösen Hautaffektionen, *Monatschr. f. Kinderh.*, 1904, ii, 57.

3. Finkelstein, H.: *Ztschr. f. Kinderh.*, 1913, viii, 1.

4. Birk, W.: Ueber den Magnesium-Umsatz des Säuglings, *Jahrb. f. Kinderh.*, 1907, lxvi, 300.

5. Meyer, L. F.: Zur Kenntnis des Mineral-Stoffwechsels im Säuglings-Alter, *Biochem. Ztschr.*, 1908, xii, 422.

Talbot⁶ in an interesting series of cases reported before this Section two years ago showed that in peritoneal tuberculosis, fat absorption was markedly diminished. This, he believes, is explained by blocking of the lymphatic channels leading from the intestinal tract by the inflammatory reaction to the tuberculous infection. Whether decreased power of fat absorption exists in other of the common forms of tuberculosis has (with the exception of a single case reported by Freund⁷) not been determined. This study is concerned with this particular phase.

The amount of material presented is not large but was carefully selected with special reference to patients in definitely active stages of the disease. The ages of the children ranged between 2½ and 10 years.

TABLE 1.—RESULTS IN SERIES A, CHILDREN FED ON FAT-RICH DIET (BUTTER CREAM, MILK, EGGS) WITH SMALL AMOUNT OF CARBOHYDRATE (BREAD)

Cases	Fat Intake in gm.	Fat Excreted gm.	Loss of Fat Per Cent.	Type of Tuberculosis
1	450.5	26.9	5.9	Pulmonary.
2	429.0	7.5	1.6	Pulmonary.
3	473.2	22.6	4.5	Pulmonary.
4	422.1	18.6	4.4	Pulmonary and glandular.
5	382.4	46.8	12.2	Pulmonary
6	298.3	30.0	10.7	Pulmonary and glandular.
7	473.2	18.1	3.8	Pulmonary and glandular.
8	404.2	10.6	2.6	Pulmonary and glandular.
9	391.7	42.6	10.9	Glandular.
10	430.0	40.5	10.7	Glandular.
11	410.3	30.8	7.5	Glandular.
12	455.1	20.3	4.2	Bone.
13	423.9	15.4	3.6	Bone.
14	361.5	59.3	16.6	Pulmonary, bone and glandular.
15	457.1	21.3	4.6	Pulmonary and peritoneal.

It is an interesting coincidence that eleven out of the fifteen cases reported were distinctly of the exudative or scrofulous type, showing how frequently this condition and tuberculosis are associated. In several of the cases manifestations had existed since infancy; in others they had become particularly pronounced during the stay at the hospital. An exclusively fat-rich diet consisting of cream, milk,

6. Talbot, Fritz B.: Tuberculosis of the Mesenteric Glands in Infants and Young Children, Its Effect on Absorption, *AM. JOUR. DIS. CHILD.*, July, 1912, xi, p. 49; Physiology and Pathology of the Digestion of Fat in Infancy, *AM. JOUR. DIS. CHILD.*, March, 1911, p. 173.

7. Freund, Walther: Physiologie und Pathologie des Fettstoffwechsels im Kindesalter, *Ergebn. d. inn. Med. u. Kinderheilk.*, 1909, iii, 139.

butter and eggs with a small addition of carbohydrate, in the form of bread, was given in the larger series, A, consisting of fifteen cases and the same diet with larger addition of carbohydrate in the form of sugar, bread and vegetables given in a smaller series, B, consisting of five cases. The diet in each case was given for a period of several days. The fat determinations in both the food and the feces were carried out according to the methods described by Talbot and also one described by Folin and Wentworth.⁸ Both methods gave good results and seemed sufficiently accurate for a clinical study of this kind.

The series of cases reported comprises all the common forms of tuberculosis and includes four cases with pulmonary involvement alone, four with pulmonary glandular involvement, three with pronounced glandular involvement only, three cases of bone tuberculosis, in one of which there was also marked glandular involvement and one

TABLE 2.—RESULTS IN SERIES B, CHILDREN FED ON FAT-RICH DIET WITH THE ADDITION OF LARGE AMOUNTS OF CARBOHYDRATE (BUTTER, BREAD, MILK CEREALS, EGGS, VEGETABLES)

Cases	Fat Intake gm.	Fat Excreted gm.	Loss of Fat Per Cent.	Type of Tuberculosis
1	472.5	14.4	3.0	Pulmonary.
2	476.5	10.5	2.1	Pulmonary.
8	424.9	11.9	2.7	
14	474.3	45.9	9.6	Pulmonary, bone and glandular.
15	393.8	20.5	5.2	Pulmonary and peritoneal.

in which there was pulmonary and suspected peritoneal involvement. The fat absorption is distinctly diminished only in the glandular type of tuberculosis. The stools in three of the cases showed both macroscopic and microscopic evidence of fat, considerably in excess of the normal. The same was shown by the quantitative determinations. In all the other forms of tuberculosis the fat absorption very nearly approached the normal.

The one case suspected as peritoneal showed good fat absorption. Series B brought out the interesting fact that the fat absorption was if anything improved by the addition of certain amounts of carbohydrate to the diet.

The results of so small a series of cases are probably not sufficient to warrant extensive conclusions. They do seem to show, however,

8. Folin, O., and Wentworth, A. H.: A New Method for the Determination of Fat and Fatty Acids in the Feces, *Jour. Biol. Chem.*, 1909, vii, 421.

that fat absorption in most of the common forms of tuberculosis is practically normal and is likely to be diminished only in those cases in which there is extensive glandular and lymphatic involvement.

If it were a question of fat absorption only, high fat feeding would not be contra-indicated in most forms of tuberculosis.

To what extent scrofulous or exudative manifestations, apparently unfavorably influenced by fat-rich food, should influence the diet of the tuberculous child is a question which the individual case must determine. The presence of the exudative condition apparently does not influence fat absorption.

Experimental and clinical evidence both seem to show that a diet which insures the largest amount of fat deposit in the tissue, with the least retention of water, is the one most beneficial to the tuberculous child.

CASE REPORTS

CASE 1.—Dorothy F., aged 10, schoolgirl. Admitted to the City Hospital Tuberculosis Pavilion in March. An outside physician had diagnosed pulmonary tuberculosis. She has not been well for some time and has had night sweats, afternoon rise of temperature, considerable cough and expectoration. Tubercle bacilli were found in the sputum. Her bowels are regular and not loose. The appetite is fair. She has been fed on fat-rich diet, especially cream, eggs and cocoa, on account of suspected lung trouble. Her father is living and well. The mother died four years ago of tuberculosis. Two brothers died of tuberculosis. She has had mumps, measles and pertussis two years ago and has not been well since the attack of pertussis. Some eczema was present during early childhood.

Physical examination shows a fairly well-nourished child with flabby muscular tone, dry skin, evidences of eczematous eruption back of the ears, and general glandular enlargement, especially of the cervical glands of the neck. The head is negative. The teeth are carious. There is some hypertrophy of the tonsils, also adenoid tissue. The chest is flat; the intercostal glands are slightly enlarged. Dulness is pronounced on the right side. Dry, crepitant râles are heard over that side and some over both lungs posteriorly. The abdominal walls are flabby. The liver is half an inch below the costal margin. The spleen is not palpable. No masses are felt in the abdomen. The extremities are quite emaciated. All reflexes are present. The tuberculin reaction is very pronounced.

CASE 2.—Amanda B., aged 8 years. Admitted to the City Hospital Tuberculosis Pavilion in February. The child was sent to the "fresh-air camp" two years ago with a diagnosis of incipient tuberculosis, one sister having just died of the disease. The patient has not been well since that time. She coughs a good deal and expectorates. Tubercle bacilli were found. There is afternoon rise of temperature. Anorexia is pronounced and she has not been gaining. Her father died of diphtheria. The mother is rheumatic and has a chronic cough. Two sisters died of tuberculosis within the last two years. The patient has had pertussis, diphtheria, measles, and scarlet fever. She has never had diarrhea and has been on a fat-rich diet, especially cocoa, eggs and cream, for the last two years.

Physical examination shows an undernourished child with pronounced pallor. The color of the skin is sallow and the skin is dry and rough. There are some eczematous patches on the legs and dry crusting on the scalp. Glandular enlargement is general. The glands of the neck and inguinal region are especi-

ally large. The throat shows general hypertrophy, both of the tonsils and of the tissue in the posterior pharyngeal wall. The chest is fairly well formed. There is some dullness over the left lower lobe posteriorly. Crepitant râles are heard throughout both lungs. The abdomen is not prominent. The liver and spleen are not palpable. No masses are felt in the abdomen. The extremities are negative. The von Pirquet reaction is pronouncedly positive.

CASE 3.—Alexander B., aged 5. Admitted to the City Hospital Tuberculosis Pavilion in May. The complaint is a chronic cough with expectoration and night sweats. Tubercle bacilli had been found. The child has had measles with two attacks of pneumonia following and has not been well since then. He continually has slight hoarseness and afternoon rise of temperature. The father is living and well. The mother has tuberculosis of the larynx and pulmonary involvement. The child has had marked anorexia and is generally constipated. The diet, for some time, has consisted principally of fats, especially milk, cream and eggs.

Physical examination shows a frail, under-nourished child, with flabby muscular tone, a clear sallow skin and general glandular enlargement. The throat is negative, the chest flat. The resonance is fair. A few crepitant râles are heard over both lungs posteriorly; de la Camp's area is dull. Large intercostal glands are palpable. The heart is normal. The abdominal walls are flaccid. The liver and spleen are not palpable. Some large mesenteric glands are palpable. The extremities are much emaciated. The reflexes are sluggish. The von Pirquet reaction is very positive.

CASE 4.—Herbert B., aged 5. Admitted to the City Hospital Tuberculosis Pavilion in April with a diagnosis of pulmonary tuberculosis. There is some cough and expectoration. Bacilli were found in the sputum. The father and mother both have active open tuberculosis. Three brothers also are all tuberculous. The child had measles and pertussis and did not recover well. He is generally constipated and has afternoon rises of temperature. The appetite is fair. He spends the summer at the fresh-air camp and has for some time been fed fat-rich diet, that is, milk, eggs and cocoa.

Physical examination shows a moderately well-nourished child, with flabby muscular tone. The skin is dry. He has had marked blepharitis marginalis. Different parts of the body show tendency to eczematous eruption. The cheeks are highly flushed. Glandular enlargement is general. The tonsils and pharyngeal tissues are hypertrophied. Eyes, ears and nose are negative. The chest is fairly well formed, has good expansion and fair resonance, except over de la Camp's area. A few dry crepitant râles are heard over both lungs posteriorly. The heart is normal; the abdominal walls are soft; no masses or areas of tenderness are palpable. The extremities are somewhat emaciated, otherwise negative. Von Pirquet's reaction is markedly positive.

CASE 5.—Irene L., aged 7. Admitted to the City Hospital Tuberculosis Pavilion in May with a diagnosis of pulmonary and glandular tuberculosis. She has coughed for some time, expectorated, and is losing in weight. Tubercle bacilli were found in the sputum. She has afternoon temperatures. Her father is living and well. The mother died of tuberculosis. The child has had pertussis. Adenoids and tonsils were removed a year ago. She was a pronounced mouth-breather and had eczematous eruptions, blepharitis marginalis, etc., all her life. She has no diarrhea, but is generally constipated. Her diet for the last two years has principally consisted of fats in the form of milk, cream and eggs.

Physical examination shows a pale, under-nourished child, with eczematous eruptions on different portions of the body. Slight adenitis of the neck and very marked general glandular enlargement are present. Her eyes show blepharitis marginalis. The throat is negative. The chest is well formed; expansion on the right side is diminished, the vocal fremitus increased. There is some dullness on percussion over the right side. A few dry, crepitant râles

are heard over the right side in the clavicular space. The heart is normal; the abdominal walls are flaccid. The liver is below the costal margin. The spleen is not felt. Some large mesenteric glands are easily palpable. They are not tender. The extremities are negative. Von Pirquet's test is markedly positive.

CASE 6.—Einar N., aged 3. Admitted to the tuberculosis pavilion in May with a diagnosis of pulmonary and glandular tuberculosis. He has been coughing for some time and is steadily losing in weight. Afternoon rises in temperature and anorexia are constant symptoms. His mother died of tuberculosis a year ago. The child has had measles and mumps. He has always had marked seborrhea and some eczematous eruption. The bowels are regular. On account of the steady loss in weight the child has had a diet consisting largely of cream, eggs and cocoa in order to "build him up."

Physical examination shows a frail, under-nourished child. His color is fair. The skin is dry; seborrhea is marked; "scrofulous habitus" is exquisite. There is general glandular enlargement. The throat shows some hypertrophy of the tissues. The chest is flat. There are no definite areas of dulness except over *de la Camp's* area. A few dry, crepitant râles are heard over both lungs posteriorly. The heart is normal. The abdominal walls are very soft. The liver and spleen are not felt. Large mesenteric glands are easily palpable. They are not tender. The extremities are very emaciated. Von Pirquet's reaction is very positive.

CASE 7.—Pauline B., aged 9. Admitted to the tuberculosis pavilion in May with a diagnosis of pulmonary and possibly glandular tuberculosis. She had pneumonia two years ago, and measles and pertussis a year ago. She has coughed since then and has steadily been losing weight. Tubercle bacilli were found. Afternoon temperature rises are constantly present. The mother has active tuberculosis and three brothers are positively tuberculous. The child has frequently had skin eruptions and chronic blepharitis marginalis. She has never had diarrhea. The diet consists of food rich in fat.

Physical examination shows a pale, under-nourished child with pronounced "phthisical habitus." Her skin is clear. The glands of the neck are very large. Pronounced blepharitis marginalis is present. The throat is negative. Tonsils and adenoids were removed a year ago. The chest is rather flat. There is marked distention of the veins on the chest wall. The breathing is shallow. Some dulness, extending downward, is present in the left axilla. Dry, crepitant râles are heard over this area, also over both lungs posteriorly, and in the right apex. The heart is normal. The abdominal walls are soft. The liver and spleen are not felt. No masses are palpable. The extremities are very emaciated. All reflexes are sluggish. Von Pirquet reaction is markedly positive.

CASE 8.—John G., aged 6. Admitted to the tuberculosis pavilion in April with a diagnosis of pulmonary and glandular tuberculosis. He had measles eighteen months ago and has not been well since. He coughs a great deal, is losing in weight, sweats profusely at night and has afternoon rises of temperature. His father died of tuberculosis three years ago; the mother is at Hope-well Hospital with active tuberculosis. A sister has active tuberculosis. The child has had marked blepharitis marginalis and eczematous eruptions for the past five years, and attacks of phlyctenular conjunctivitis for the past two years. He has had several broken-down glands. The bowels are generally regular. The child has been in fresh-air camps and hospitals most of the time for the past year and a half. He has principally a fat-rich diet.

Physical examination shows a poorly-nourished child, with flabby, muscular tone. The skin is dry, showing eczematous eruptions on different portions of the body and marked seborrhea. There are old scars of broken-down glands about the neck and under the left eye. General glandular enlargement is pronounced. Eyes show evidence of phlyctenular ulcers. The tonsils are hypertrophied and adenoid tissue is pronounced. The chest is flat. Dulness extends

over both lungs posteriorly. Crepitant râles are heard on deep respiration, especially over the left side. The abdominal walls are soft; the liver and spleen not felt. No masses are palpable. The extremities are very emaciated. There are some scars on both legs from fistulous glands. The von Pirquet reaction is markedly positive.

CASE 9.—Jessie G., aged 2. Admitted to the tuberculosis pavilion in April with a diagnosis of glandular tuberculosis. She is the sister of Patient 8. There has been no definite, acute illness, but she has not been well since birth. Chronic bronchitis began after the first year and also suppurating glands in different parts of the body. She is not gaining and has been an inmate of fresh-air camps and hospitals for the past year. Her bowels are never loose. She has practically always been on a fat-rich diet. Marked crusta lactea is present, also eczematous eruptions on different portions of the body. Blepharitis marginalis is present. She has afternoon rises of temperature and gives a very positive von Pirquet reaction.

Physical examination shows a pale, moderately well-nourished child. The skin is dry and there are some eczematous eruptions on the face and neck. Adenopathy is general. Scars of broken-down glands show on the neck and legs. The child is a mouth-breather. The tonsils are hypertrophied and there is much adenoid tissue. Her chest is well formed; the lungs are clear throughout. The heart is normal. The abdominal walls have good tone. The liver and spleen cannot be felt. Some small masses are palpable in the lower abdomen. They are apparently enlarged mesenteric glands. The extremities are negative except for scars. Von Pirquet reaction is markedly positive.

CASE 10.—Philip St. J., aged 3½. Admitted to the tuberculosis pavilion during October of the last year with a diagnosis of glandular tuberculosis. He coughs a good deal, has afternoon rises of temperature and is losing weight. Several abscesses developed on the right side of the neck, also on the right cheek and both arms. His father is living and well. The mother died of tuberculosis, and one sister is tuberculous. The child has had no previous acute illness, but has had scrofulous manifestations, eczema, etc., since infancy. Since the child's admission to the hospital the diet has consisted of mixed food with a liberal amount of fat. She is generally constipated.

Physical examination shows a pale well-nourished child. The muscular tone is fair, the skin is dry and shows some seborrhea. There is pronounced general adenopathy, especially adenitis of the right side of the neck. Scars of healed fistulas are present. A large scar on the right cheek is the result of an ulcer. The throat is negative. The chest is well formed, the resonance over the right lung diminished. Crepitant râles are heard in the right apex anteriorly, and coarse, moist râles over both lungs posteriorly. The abdominal walls are soft, the liver and spleen not felt. No masses are palpable. The extremities show scars of recently healed ulcers on both ankles and both forearms. The von Pirquet reaction is markedly positive.

CASE 11.—Mary D., aged 3. Admitted to the tuberculosis pavilion in April with a diagnosis of glandular tuberculosis. For the past nine months she has had "cold" abscesses about the neck, face and on several extremities. The child has a chronic cough, afternoon rise of temperature and is losing in weight. The mother is at Hopewell Hospital with active, open tuberculosis. The child has had no previous acute illness but has always had pronounced exudative or scrofulous manifestations, phlyctenular ulcers, crusta lactea, etc.

Physical examination shows an under-nourished child, with flabby muscular tone. The skin is dry and rough. Adenitis of the neck is pronounced. Scars of healed, broken-down glands show on the left side of the neck and face. Several scars show on the left leg and both arms. There is marked general adenopathy. The eyes show evidence of phlyctenular ulceration and blepharitis marginalis. The tonsils are markedly hypertrophied. The chest is well formed. A few râles are heard over both lungs posteriorly. Dulness is heard over

de la Camp's area and over the base of the right lung, posteriorly. The abdominal walls are soft; the liver and spleen not palpable. No definite masses are felt in the abdomen. Extremities show scars of healed fistulas. Von Pirquet reaction is markedly positive.

CASE 12.—Esther O., aged 10. Admitted to the tuberculosis pavilion with a diagnosis of bone tuberculosis. She developed lameness and pain in the left hip and knee shortly after her mother's death from tuberculosis, five years ago. The symptoms increased in severity. Open, active tuberculosis manifested itself two years ago. Extensive glandular involvement developed with wasting and afternoon rise of temperature. The child passed the last two years mostly in fresh-air camps and hospitals and has had principally a fat-rich diet. She has never had diarrhea. She has had diphtheria and an attack of pneumonia three years ago, and has had "scrofulous" manifestations, blepharitis marginalis, phlyctenular ulcers, etc.

Physical examination shows a fairly well-nourished child, with good muscular tone. The skin is dry and shows some seborrhea. Pronounced cervical adenitis and general glandular enlargement are present. The eyes show phlyctenular ulcers on both conjunctivae and marked blepharitis marginalis. The chest is well formed. There are no definite areas of dullness. A few crepitant râles are heard over the lower lobe of the left lung. The heart is normal; the abdomen is firm. The liver and spleen are not palpable. No masses are felt in the abdomen. The left leg is markedly shortened and somewhat atrophied. The child limps decidedly. A scar of a fistulous opening shows below the hip-joint. The von Pirquet reaction is very positive.

CASE 13.—William R., aged 12. Admitted to the tuberculosis pavilion in April with a diagnosis of tuberculous hip-joint. The trouble began four years ago after a severe attack of measles. He also had a severe fall at that time and injured his left hip. Much pain developed subsequently in the hip-joint and knee. He is decidedly lame. The leg is shortened and somewhat atrophied. No fistulas are present. The child has daily rises of temperature, tires easily and has night sweats. One sister has been ill for some time with active tuberculosis. For the last two months he has been on a mixed diet with liberal quantities of fats. His bowels are regular.

Physical examination shows a fairly well-nourished child with flabby muscular tone. The skin is clear except for slight eczematous patches over the eyes. The glands are large, especially the cervical. A scar from a healed, broken-down gland is visible on the right side of the neck. The chest is flat and there are no areas of dullness. The lungs seem clear throughout. The heart is normal. The abdominal walls are soft; the liver and spleen are not felt. Numerous small masses, apparently mesenteric glands, are palpable, especially in the lower part of the abdomen. His left leg shows limited motion, is shorter than the right and is somewhat atrophied. Pressure on the head of the femur causes pain. The von Pirquet reaction is markedly positive.

CASE 14.—Ralph B., aged 10. Admitted to the tuberculosis pavilion in March with a diagnosis of pulmonary, bone and glandular tuberculosis. The father, mother, paternal grandparents, and three brothers are all actively tuberculous. The child had typhoid fever two years ago. Cough, expectoration, loss of weight and afternoon temperature date from that time. A year ago the child fell, injuring the left hip. Open bone tuberculosis developed shortly afterward and is still active. The child has always had scrofulous or exudative manifestations. The past two years have been spent mostly in fresh-air camps and hospitals. On account of his "weak constitution" his food has always consisted principally of fat-rich food. The child often has attacks of diarrhea.

Physical examination shows a pale under-nourished child, with flabby, muscular tone. The skin is dry and eczematous eruptions show on different portions of the body. Cervical adenitis and general glandular enlargement is pronounced. Blepharitis marginalis is present in both eyes and a phlyctenular ulcer shows

on the left conjunctiva. Adenoid tissue is abundant and the tonsils are very large. The chest is flat and slightly deformed. There is a dullness over the left lower lobe. Bronchial breathing with dry, crepitant râles are heard at that point. Numerous crepitant râles are heard over both lungs posteriorly. The abdominal walls are soft. The liver and spleen are not felt. Enlarged mesenteric glands are palpable in different parts of the abdomen. The left leg has limited motion. There is apparently no shortening or atrophy. A fistulous opening shows near the greater trochanter. The von Pirquet reaction is markedly positive.

CASE 15.—Mary S., aged 8. Admitted to the tuberculosis pavilion during November of the past year with a diagnosis of pulmonary and possibly peritoneal tuberculosis. There is no history of tuberculosis in the family. The child has never been strong, has always coughed a great deal, and did not gain well. The abdominal symptoms developed last summer following an attack of diphtheria. She has had frequent attacks of pain with alternating constipation or diarrhea. Blood is frequently passed in the stool. The abdomen is generally quite distended, partly due to gas and probably some fluid. The child is losing in weight. She has afternoon fever constantly. She has always had large quantities of cow's milk. Since her stay in the hospital she has been put on a mixed diet.

Physical examination shows a pale under-nourished child, with flabby muscular tone. Her skin is pale and dry. There is general adenopathy. The throat is negative. The chest is somewhat barrel-shaped. Large intercostal glands are palpable. Dullness is present over de la Camp's area. A few dry, crepitant râles are present over both lungs, posteriorly. The abdomen is very prominent; a tympanitic note is heard on percussion with some dullness in both flanks. There are no definite evidences of fluid. Large mesenteric glands are palpable in the lower quadrants of the abdomen. The liver and spleen are not felt. The extremities are very emaciated. The von Pirquet reaction is markedly positive. The stools at the present time show no macroscopic or microscopic evidence of excess of fat.

820 Donaldson Building.

IN MEMORIAM THOMAS MORGAN ROTCH, CHARLES PICKERING PUTNAM, FREDERICK FORCHHEIMER

THOMAS MORGAN ROTCH

Rotch wrote in 1873, "The Emigration of the White Corpuscle in Inflammation," an essay to which was awarded the first prize of the Boylston Medical Society for 1873; and in 1878, "Absence of Resonance in the Fifth Right Intercostal Space, Diagnostic of Pericardial Effusion," for the Massachusetts Medical Society.

The first impressed me as the work of a young man—he was born Dec. 9, 1849—given to study and scientific ambition; the second told of good observation and practical tact. That is why I invited him to act as secretary to the Pediatric Section of the American Medical Association which was to be founded. Never was a place accepted with more eagerness and filled with more capacity and success.

The meeting of the American Medical Association of 1880 took place at Richmond, Va. In that year and at that place there was founded the Section on Diseases of Children which has existed these thirty-four years with increased vigor and usefulness. Twenty years previously a futile attempt had been made to establish such a section in the New York Academy of Medicine. A second attempt was made in 1885, which has proved a success. This American Pediatric Society of yours has existed since 1888. You all know that pediatrics, since the second president, J. Lewis Smith, and Thomas M. Rotch, the third, has evolved into a powerful and vigorous body, nor are you unacquainted with the great influence Dr. Thomas M. Rotch has wielded in the development and fertility of pediatrics in American Medicine, which had to overcome more obstacles in this country of ours than in any country on the globe with the exception of Great Britain. Reactionary powers, such as antivivisectionism, antivaccinationism, sectarianism, and the enemies of autopsies, together with the lack of thoughtfulness and of perfect and uniform education in professional and well-to-do circles, such as those of clergymen, lawyers and legislators, have combined to cripple or obstruct the science and art of medicine in the United States.

After his return in 1876 from Europe where he studied in Berlin, Vienna and Heidelberg, he practiced in Boston, always with a view to the welfare of children and the teaching of their physiology and diseases. The pediatric department of Harvard University owes him

* Delivered in the meeting of the American Pediatric Society, Stockbridge, Mass., May, 1914.

everything. That university was almost the first in America to establish a special chair for pediatrics as the proper reward for his incessant labors in that branch of medicine. It has happened in connection with that fact, and it is characteristic of his modesty, that Rotch asserted that the administration of Harvard was induced to raise that chair to full professorship only by the appreciative mention in the introduction to the first volume of Keating's *Cyclopedia of Pediatrics*, of pediatric work and the necessity of establishing greater facilities for the study of the diseases of the young.

In this movement, Harvard was preceded by one medical school only. That was a small "New York Medical College" of East Thirtieth Street, New York. Its reorganization in 1860 included a regular professorship for the diseases of children, and created the first regular general bedside instruction under its own roof. Both of these advancements died (but should not be forgotten in the history of American medical education) when the school had to be closed in the last year of the Civil War.

The Archives of Pediatrics of 1887 and the medical publications of the Harvard Medical School of the same year contained a paper of Rotch on "The Artificial Feeding of Infants." One on "Breast Milk" was published in 1890, a "Presidential Address" in 1891. They were followed by a paper on milk laboratories in 1893, on substitute feeding in 1896, on modified milk in 1897, on the history of percentage feeding, another on pasteurization of milk for public sale, a third one on Roentgen ray in 1907. Meanwhile, since 1896, he published successive editions of his large book which he called "Pediatrics."

His labor was not limited to the study of diet. He wrote on acute exanthems in 1897, on the perforation of the stomach in an infant 7 weeks old, in 1899, on rachischisis in 1900, on infantile scurbutus, on the study of pediatrics, on tuberculous peritonitis in 1903, on diarrhea in 1904, on gonorrhea and syphilis in 1907.

Nor was he working alone; his endeavor was often to have others, usually young men, cooperate with him. He published with Cushing, decapsulation of both kidneys; with Dunn, pulmonary or osteoarthropathy; with Floyd, opsonic index and tuberculin test; with George, normal living anatomy, and osteomyelitis; with Holt, nomenclature of diseases of the gastro-enteric tract; with Ladd, pernicious anemia; with Low, blood cultures; with Murphy, gastro-enteric obstruction.

Dr. Rotch's labors and activities were so many and so successful as to render his positions and places of honor and responsibility insignificant. He was one of those who are counted by what they do and not by what people say of them. Still his honors were many and more than what J. McKeen Cattell enumerates in his "American Men of Science." The following lines refer to Rotch:

A.B., Harvard, 1870; professor pediatrics, Harvard, 1893; consulting physician Boston City Hospital; visiting physician Children's Hospital; medical director Infant Hospital; consulting physician Infant Hospital, London, Eng.; Fellow of the Association of American Physicians, of the American Pediatric Society (once its president), American Medical Association, Massachusetts Medical Society, Suffolk District Medical Society (once its president). Let this, however, suffice.

Dr. Rotch is one of the men whose greatness is won by hard work in a limited sphere. He appreciated the boundary lines restricting everybody, but he felt from the beginning of his career the necessity of constructive work. That is why a large number of his papers are dedicated to the subjects of infant feeding, and particularly percentage feeding. His call to present to the British Medical Association the methods of what was considered the American method of infant feeding was the first proof of the impression his personality and searching had made far and wide, and the foundation, in London, of a milk laboratory like that established by Rotch in Boston. It is well known to you all that the first Boston Laboratory was not installed in America until Rotch had proved to the profession in New York and other cities the desirability, or rather indispensibility, of clean milk of high-grade for infant feeding. That example became the teacher both of the profession and the public, aye, even the trade, whose interest is believed by many to be best served by the selling of the worst possible article for the highest possible price, and whose virtues are often considered commensurate with the dangers or fears of punitive measures. Nobody knew that better than Rotch; that is why he never failed in his suspecting watchfulness in connection with milk laboratories.

I now quote a line from Dr. Dunn's review in the *Boston Medical and Surgical Journal*:

"For' the last twenty years Professor Rotch was much interested in developing the work of the Infant Hospital, the first hospital in this country to admit patients restricted to the first two years of life."

This is only part of the initiative work of Dr. Rotch. It must be left to those who are intimate with his daily life and exertions to record in appropriate terms and with sufficient energy the great merits of Rotch in connection with his searching and working in the two large hospitals he controlled. Now the number of constructive physicians in this country is not large. Not one of them should be buried in silence; least of them a man who has genuine and permanent merits. These were his vast knowledge, enthusiastic industry, clear and logical expression and other gifts of a great clinical teacher.

These gifts were increasingly developed with every year of his teaching life. The disproportioned chapters of his great "Pediatrics" were improved from edition to edition. The first of them, to a large extent, indeed, one-fourth of the book, was filled with the feeding of infants. Gradually it became a hand-book of greater usefulness and proper proportions. With years and learning, guided by his watchful brain and warm heart, he became more statesmanlike in his views and researches. His big book, "The Living Anatomy and Pathology of Early Life as Shown by the Roentgen Method," was pervaded by a humane and humanistic study of the growing child. He gave a distinct discrimination between the actual and chronological age of the growing child, insisting on the cautious examination of a child wishing or compelled to enter on manual labor, according to the anatomic development of the body as exhibited by his osseous growth. Rotch worked assiduously and successfully for years, giving credit to writers who had worked in the same direction. It is exactly that class of research and that class of students that will prove the blessing of the cooperation of science, sociology and conscientiousness.

It is quite possible that Rotch will be mostly remembered by the permanent influence his hospitals will exert on the health of thousands of patients, and on the ever-living schooling which students and doctors will derive from his creations. This influence I estimate much higher than the immediate good done to the sick. This value to the profession is greater than that which would accrue from similar work performed by men equally gifted or more personally ambitious. Dr. Rotch was a general practitioner, a great searcher, and to all his work he added the outflow of his kind and humane heart and the appreciation of the fact that only a good man can be a great and good doctor. That is what Hippocrates meant when he said that where there is love of our calling there is love of mankind, or Nothnagel when he said before closing his eyes: "Only a good man will be a good doctor." That is what Rotch *did*. Though being given to accurate research he never severed it from the dictates of conscience and humanity. No medical man who does research work alone, laboratory work on dead tissue alone, will ever rival in his results, the warm-hearted person who studies the soul of the patient who is under observation, and estimates the innermost folds of a man's heart who clamors for relief. The human suffering body is to a man like Rotch much more than his physiologic make-up.

There is still more to Rotch's credit. There are those who disagreed with him in regard to his theories and teaching on the feeding of babies. Those here and outside who find fault with him should not forget what they inherited from him before he died. Our inheri-

tance is the impressive teaching of the necessity of studying the infant and child. He belongs to the few who studied and taught pediatrics because they could not help it. No distress of his own, stoutly borne because fate brought it, made him shirk or interrupt the hard work required to accomplish his beneficial ends. Let nobody forget that it was he amongst a few who in America raised pediatrics to the rank of a genuine science and humane practice. I wish my American colleagues would soon appreciate the fact that the young men you send to certain European centers to learn medical science and morals, find their goal more often after their return, when they meet the good and great men represented in this and other scientific bodies.

A. JACOBI.

CHARLES PICKERING PUTNAM

Dr. Charles Pickering Putnam, for many years a member of this Society and its president in 1909, died April 23 last, in his seventieth year. He was one of a family of physicians, his father having been Dr. Charles Gideon Putnam, and his grandfather, Dr. James Jackson. He graduated from Harvard College in 1865 and from the Harvard Medical School in 1869. After studying for a time in Germany, he began the practice of his profession in Boston in 1871. He was a general practitioner, but for many years made a specialty of pediatrics. He was a lecturer on Diseases of Children at the Harvard Medical School from 1873-1875, and a clinical instructor in the same subject until 1880. At this time he also did some excellent pioneer work in orthopedics.

He served the Boston Dispensary as district physician from 1871 to 1873, and as orthopedic surgeon from 1873 to 1876. He became physician to the Massachusetts Infant Asylum in 1875, and was also president of its board of trustees from 1898 to 1910. He was chiefly instrumental in the development of the boarding-out system established by this hospital many years ago.

Dr. Putnam was from the very beginning of his career the leader in Boston in charitable and social work connected with children. He was one of the founders, in 1873, of the Boston Society for the Relief of Destitute Mothers and Infants, which was a pioneer in establishing the policy of keeping mother and child together. He was president of this society from 1904 until his death. He was one of those who, in 1879, took part in the movement for establishing the Associated Charities of Boston, the second charity organization society in this country. He always took a very active part in its work, and was its president since 1907.

Dr. Putnam took a leading part for many years in all the movements for the care of the poor and of the neglected and delinquent children of Boston. He held many public positions, among the most important of which was that of chairman of the Board of Children's Institutions, from 1902 to 1911. His work was never properly appreciated and he was frequently misjudged, largely because the public and the politicians were unable to understand the absolute honesty of the man and to realize that he was always working for the good of the community and not for his own advantage or preferment.

He was one of the incorporators of the Boston Medical Library, in 1875, and served on important committees of this institution until his death. He helped to organize and carry on the Directory for Nurses established by this institution and at the time of his death was in charge of it. This was the first directory for nurses established in Boston.

He was a tireless worker, and a remarkable organizer. He had, in addition, the unusual faculty of interesting others and of making them work as hard as he did himself.

He was the ideal family physician, beloved by all his patients. No one can ever quite fill his place for them. No one man can take his place in the community and in public work. It will take many men to do that.

JOHN LOVETT MORSE,
CHARLES HUNTER DUNN.

FREDERICK FORCHHEIMER

"And so he dwelt among men, physician and sage. He served them, loving them, healing them, sick or maimed."

Truly this was a life of loving service; and surely there came the reward: he was the beloved physician.

Frederick Forchheimer was a man of unusual attainments, and of noteworthy achievements. A great clinician with all that it implies, a profound scholar, a wise teacher, he was; and with it all a man of wondrous charm. He had to a most uncommon degree the quality of personal magnetism which drew to him countless friends and held them fast. To know him well was to love him; and to have his affection was to have that which made its possessor proud. His was a busy life, and yet there was always time for kindness—in thought and deed—for those who needed him.

He was one of the rare souls who found his greatest pleasure in the happiness he could bring to others.

An eminently successful practitioner, he remained always an idealist in medicine.

His influence in the lay world was tremendous—and always for good. His position in the profession was that of earnest student, of painstaking teacher, of wise counselor to whom all might turn for aid.

One of the founders of this Society, one of the pioneer teachers of pediatrics in this country, he retained always his special interest in this branch of his work. His was the broad outlook, and his the comprehensive grasp. The exactions of an arduous practice left him little time for purely research work in the later years of his life, but his interest in scientific medicine was ever keen, his knowledge of its attainments always sure.

To the medical world at large Frederick Forchheimer was known and favorably known, by his books.

To the multitude to whom he gave his medical skill, ever unstintingly, ever unselfishly, he came as a carrier of cheer and helpfulness.

And to those—and they are many—who were privileged to call him friend, he was an ever-present inspiration. The rewards of his well-spent life were many. Not the least of them was the love that came to him from all who knew him.

B. K. RACHFORD,
C. G. JENNINGS,
ALFRED FRIEDLANDER.

PROGRESS IN PEDIATRICS

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BLOOD-PRESSURE IN NORMAL CHILDREN *

C. F. JUDSON, M.D., AND PERCIVAL NICHOLSON, M.D.
PHILADELPHIA ARDMORE, PA.

In pediatrics the amount of research in blood-pressure has been limited, and so far, but little of real value has been developed. While blood-pressure determination in adults is conceded to be of inestimable value, many practitioners consider that it has little or no significance in children. This statement is not reasonable unless we assume that there are many additional factors, especially in technic, interfering with accurate readings, and that such wide variations are encountered as to vitiate the results.

We have undertaken a series of studies in normal children, in order to determine whether a standard of blood-pressure could be established. Could such a standard be made, it would open to the pediatrician a new aid in diagnosis and prognosis and help in the treatment of a large number of diseases. Blood-pressure readings will also furnish a means of determining the physical tone of a large number of children who are below par but have no demonstrable pathologic lesion. The whole problem depends on our having an accurate and reliable means of obtaining the readings. After the attainment of a correct technic a sufficient number of observations should be taken in order to establish a standard.

The blood-pressure of children, as of adults, depends on four main factors: the contracting force and rate of the heart; the peripheral resistance of the arterioles and capillaries; the elasticity of the vessel walls; and the character of the blood as to volume, viscosity, etc.

The contracting force and rate of the heart is the most important factor. Owing to the relatively larger, more elastic, and distensible arterioles and capillaries found in children, the peripheral resistance is less marked than in adults, and the vessel-walls are in a less stable state of equilibrium. This simply means that the systolic blood-pressure is a more direct representation of the work of the heart than in the adult. The importance of the vasomotor system must not be overlooked as one of the main factors causing variations in blood-

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

pressure in childhood. The volume and viscosity of the blood are as a rule of slight importance.

All blood-pressure determinations are influenced by certain physiologic factors. The systolic blood-pressure varies with the increasing age of the child. Blood-pressure changes with alterations in weight and, in children of the same age, varies according to height. The influence of sex is less than in the adult, with slightly higher readings in the males. Emotions cause an increase in pulse-rate and a consequent elevation of blood-pressure. Within fifteen or twenty minutes after meals there is a rise, and a fall again in three-quarters of an hour to an hour and a half.¹ There is a gradual fall in blood-pressure during sleep.² At the end of the day blood-pressure is higher than in the morning. There is a rise in blood-pressure following exercise, directly in proportion to the amount of muscular effort. During inspiration blood-pressure falls, to rise again during expiration. In healthy children breathing does not exert much influence except during prolonged forced and deep respiration.

Since there are more or less constant changes in blood-pressure from day to day, it is important in children, as in adults, to secure a series of observations on each individual.

Among the earlier American workers in this field was Cook,³ who used a modified Riva-Rocci instrument with a narrow 5-cm. cuff, and took observations of the systolic pressure only, using the palpation method. He did not report any diastolic readings. Stowell and Lennox Gordon⁴ have also reported systolic blood-pressure readings from a number of cases, using a 12-cm. cuff, and a mercurial instrument. Investigations on fifty-eight children were carried out by N. Oppenheim and S. Bauchwitz,⁵ using a modified Riva-Rocci apparatus with a 5-cm. cuff. They made no determinations of the diastolic pressure. A large series of observations on children by the palpation method were made by W. Kaupé,⁶ using a Riva-Rocci instrument with a 12-cm. cuff. He took as the systolic pressure the average reading at the time of disappearance and reappearance of the radial pulse to the palpating finger. The method of obtaining diastolic readings is not stated.

In Sahli's clinic an extended series of blood-pressure observations was made by P. Wolfensohn-Kriss,⁷ using a Riva-Rocci instrument

1. Loeper: *Arch. d. mal. du coeur*, 1912, p. 225.

2. Brush and Fairweather: *Am. Jour. Physiol.*, 1901, p. 199; Brooks, Harlow, and Carroll, John H.: *A Clinical Study of the Effects of Sleep and Rest on Blood-Pressure*, *Arch. Int. Med.*, August, 1912, p. 97.

3. Cook: *Am. Jour. Med. Sc.*, 1903, cxxv, 433.

4. Stowell and Gordon, Lennox: *Arch. Pediat.*, May, 1911.

5. Oppenheim, N., and Bauchwitz, S.: *Arch. f. Kinderh.*, 1905, xlii, 415.

6. Kaupé, W.: *Monatschr. f. Kinderh.*, 1910-11, ix, 257.

7. Wolfensohn-Kriss, P.: *Arch. f. Kinderh.*, 1910, liii, 332.

TABLE 1.—SYSTOLIC, DIASTOLIC AND PULSE-PRESSURE IN NORMAL CHILDREN BY THREE METHODS—AUTHORS' OBSERVATIONS *

Years	Width Cuff cm.	No. of Observa- tion	Circ. of Arm cm.	Pith-Ball			Auscultation			Erlanger Mod.			Pulse
				S. P.	D. P.	P. P.	S. P.	D. P.	P. P.	S. P.	D. P.	P. P.	
3	9	24	13.5-14.0	88.8	54.1	34.7	92.0	D 58.4 G 41.6 D 61.7	33.6	91.8	65.6	26.2	92
4	9	95	13.0-16.5	93.7	59.8	33.9	92.6	G 49.1	30.9	91.6	64.9	26.7	99
5	9	69	13.0-18.0	97.4	61.1	36.3	91.6	D 60.0 G 46.0	31.6	91.3	64.4	26.9	93
6	9	110	13.0-16.0	96.1	62.7	23.4	93.8	D 63.5 G 51.9	30.3	92.6	67.3	25.3	95
7	9	145	14.5-17.5	99.3	64.4	34.9	87.9	D 64.2 G 49.2 D 59.6	22.7	94.4	66.4	28.0	87
8	13	128	15.0-20.0	93.7	64.6	29.1	93.0	G 41.0 D 62.2	33.4	93.6	64.7	28.9	88
9	13	149	16.0-19.0	103.3	70.6	32.7	91.7	G 50.0 D 64.6	29.5	94.3	71.0	23.3	84
10	13	203	15.0-19.5	100.2	65.7	34.5	99.0	G 47.3 D 62.3	34.4	99.2	67.1	32.1	87
11	13	169	15.0-20.5	98.5	74.4	24.1	95.8	G 49.1 D 59.6	33.5	97.1	65.6	31.5	87
12	13	94	17.0-24.0	100.9	64.0	36.9	99.9	G 37.6 D 63.2	40.3	102.3	65.2	37.1	89
13	13	80	14.0-22.5	103.0	66.0	37.0	104.0	G 47.0 D 63.7	30.8	103.6	70.5	33.1	96
14	13	43	18.0-25.0	109.7	69.4	40.3	105.8	G 48.2 D 61.8	42.1	106.1	67.4	38.7	84
15	13	35	17.5-24.0	103.2	68.5	34.7	99.6	G 43.6	37.7	105.6	67.5	38.1	84

* S. P. = systolic pressure; D. P. = diastolic pressure; P. P. = pulse pressure; D. = beginning dull or fourth phase; G. = all sound gone, fifth phase.

with a 6-cm. cuff. The systolic readings were estimated by the palpation method, the diastolic readings by the change in the character of the pulse-wave to the palpating finger. She admits that the cuff used was too narrow for accurate results. A. Katzenberger⁸ made a series of 241 observations on children ranging from 4 to 14 years of age, using a mercurial instrument with an arm-band 9.5 cm. wide. All readings were taken by the auscultation method. To indicate the diastolic pressure she used the time of disappearance of all sound. She found a gradual increase in blood-pressure from 1 to 14 years, and then a sudden rise.

The most recent work of a scientific nature on blood-pressure in children is that of Mello Leitao.⁹ His observations were made on healthy infants and children up to 6 years of age. He used an Erlanger apparatus with a 6-cm. cuff, applied to the thigh and the pulse was felt in the posterior tibial artery. The use of the narrow cuff gives a considerable error, as the width of the cuff should be proportional to the circumference of the extremity used. His figures represent the most careful work on blood-pressure in infants.

In reviewing the work of previous investigators it is necessary to determine the value and accuracy of the various methods employed. The palpation method is the oldest one. It gives a fairly correct systolic pressure, but does not give accurately the diastolic pressure. The personal equation in estimating the diastolic pressure has been found so great that this method has been entirely discarded by careful observers. Otfried Müller is authority for the statement that the method of measuring the diastolic pressure by taking the time of lessened pulse-wave (as noted by palpation), is liable to an error of 28 per cent., when compared with readings taken with a manometer tube in an open artery.¹⁰ Since the blood-pressure is lower in children it is much harder to determine the time of appearance or disappearance of the pulse-wave than in adults. We feel that the observations taken by this method cannot be considered accurate.

The oscillatory method, as exemplified by the von Recklinghausen, Pachon and Erlanger apparatus, represents a step in advance. Neither the von Recklinghausen nor the Pachon instruments are recording. As they depend on the spring capsule principle they are very unreliable and require constant standardization; therefore, they will not be further considered. The Erlanger apparatus, however, is a recording instrument and not subject to inaccuracy due to usage. At first sight this apparatus seems to afford an accurate means of blood-pressure

8. Katzenberger, A.: *Ztschr. f. Kinderh.*, 1913, ix, 167.

9. Leitao, Mello: *Arch. d. méd. d. enf.*, February, 1913.

10. Müller, Otfried: *Ztschr. f. Kinderh.*, 1913, ix, 167.

determination in children, but the use of the instrument as devised by Erlanger is difficult and the results are open to question. When the systolic pressure is to be determined, the pressure in the apparatus is raised considerably above the obliteration of the radial pulse, the kymograph drum is started to rotate and the pressure in the cuff is slowly released by means of an ingenious valve. The operator must observe the needle on the drum and the height of the mercury column. At the time there is an abrupt increase in the oscillation of the needle, the observer reads the height of the mercury column and records it as the systolic pressure. Many observers have found it difficult to obtain accurately the systolic pressure by this method. When this instrument is used for the estimation of blood-pressure in children the oscillations are much smaller and the difference in the height of the oscillations is much more difficult to determine. The observation of the diastolic pressure by the continual lowering of the mercury column is open to the same objection, whereas if one releases the pressure in 5-mm. steps, as advocated by Dr. Erlanger, it takes so long for the observation that the nervousness of the child vitiates the results.

The auscultation method was introduced by Korotkoff¹¹ in 1906 and has replaced the older palpation method in adult work. It is very simple and requires no complicated apparatus. By reading the height of the mercury column at the time the first clear sound is heard (first phase), the correct systolic pressure is obtained. That this method gives accurately the systolic pressure in adults is universally recognized. In children it is not always possible to hear the sounds plainly but in the large majority of cases it can be done. Care should be taken to place the stethoscope at least 1 inch (2 cm.) below the edge of the constricting cuff. As the artery under the cuff is forced against the bone out of its normal relations, it takes at least a distance of 2 cm., or 1 inch below the cuff, before the artery returns again to its normal superficial relations so that we can get the best auscultatory results. The arm should be used whenever possible, as the artery is superficial and auscultation easy. The diastolic pressure can also be accurately determined by this method. After obtaining the systolic reading as described above, one continues to listen over the artery and soon hears a murmur (second phase), replacing the first clear thumping sound. This murmur in turn is replaced by a second tapping sound (third phase) which later becomes duller (fourth phase). Shortly thereafter all sounds disappear (fifth phase).

11. Korotkoff: *Tr. Imp. Acad. Med., St. Petersburg*, 1905, xv, 365.

Most of the more recent observers hold the view that the beginning of the fourth phase (or dull sound) denotes the time of the true diastolic pressure. The height of the mercury column at this time gives the correct reading. Schrumpf and Zabel¹² made twelve hundred observations of blood-pressure. In the majority of cases the results obtained by the auscultatory method corresponded to the results of the oscillatory method. Lang and Manswetowa¹³ determined that the diastolic pressure corresponds to the beginning of the fourth phase. Fischer holds the same view, as does also B. Zabel,¹⁴ who took the beginning of the fourth phase as synchronous with the correct diastolic pressure. Lately, Warfield,¹⁵ Taussig and Cook,¹⁶ have con-

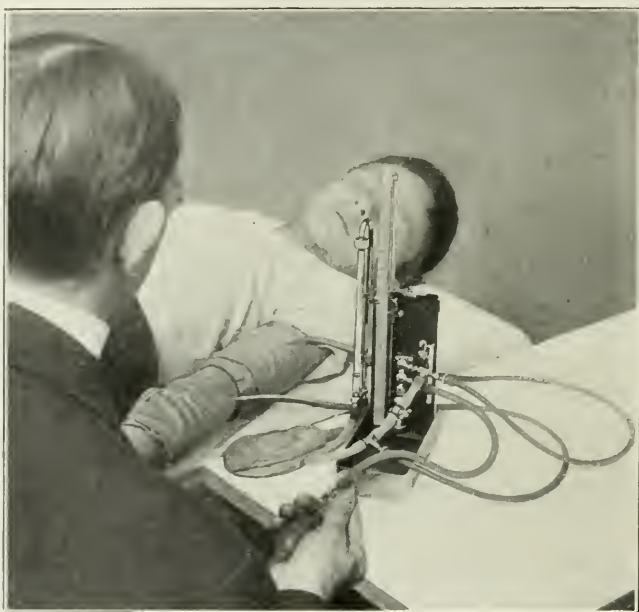


Fig. 1.—Nicholson apparatus with pith-ball attachment.

firmed these observations. Warfield conducted a series of animal experiments which proved this point. The authors are in complete accord with these views and have corroborated them in their work.

12. Schrumpf and Zabel: *München. med. Wchnschr.*, 1909, lvi, 704.

13. Lang and Manswetowa: *Deutsch. Arch. f. klin. Med.*, 1908, xciv, 441.

14. Zabel, B.: *Berl. klin. Wchnschr.*, 1909, xlv, 1352.

15. Warfield, Louis M.: *Studies in Auscultatory Blood-Pressure Phenomena. The Experimental Determination of Diastolic Pressure*, *Arch. Int. Med.*, September, 1912, p. 258; *Studies in Auscultatory Blood-Pressure Phenomena—the Chemical Determination of Diastolic Pressure*, *The Journal A. M. A.*, Oct. 4, 1913, p. 1254.

16. Taussig, Albert E., and Cook, Jerome E.: *The Determination of Diastolic Pressure in Aortic Regurgitation*, *Arch. Int. Med.*, May, 1913, p. 542.

The pith-ball apparatus was originated by Dr. Fedde¹⁷ as a means of determining diastolic pressure. It was later modified by Dr. Hoobler,¹⁸ to take both systolic and diastolic readings. This instrument was still later modified by one of us. Figure 1 shows the modified apparatus as used by us. The principle utilized in this apparatus is that of oscillation, and rests on the proven work of Sahli.

No matter what method is employed there are certain details as to the size of the cuff, etc., that are essential. Von Recklinghausen¹⁹ has shown the importance of having a cuff between 12 and 15 cm. in width for use on adults, and some investigators have emphasized the importance of the wide cuff in observations on children. With



Fig. 2.—Dr. Nicholson's modification of Erlanger apparatus.

this in mind we have taken readings with cuffs of different width under similar conditions in order to determine how great a significance is to be attached to the width of the cuff. Another detail of technic is emphasized by Schrumph and Zabel,¹² namely, that the arm-band must be applied snugly and in a completely deflated condition (especially between readings) to avoid causing congestion of the arm. The cuff must not press on the artery at the bend of the elbow. It is also important in applying the cuff to be sure that the

17. Fedde: *Med. Rec.*, New York, July 10, 1910.

18. Hoobler: *Med. Rec.*, New York, Dec. 30, 1911.

19. Von Recklinghausen: *Arch. f. exper. Path. u. Pharmakol.*, 1901, xlii, 78.

pneumatic pad is placed directly over the line of the artery. All observations must be taken as rapidly as possible, not only to avoid congestion of the extremity but also to prevent the undue excitement incident to prolonged pressure. The most opportune time is between meals, preferably in the afternoon and in the reclining position.

In the progress of our investigations it seemed advantageous to control our readings by another method. Accordingly, Dr. Nicholson modified the Erlanger apparatus in the belief that the personal equation could be practically eliminated. The modification of the Erlanger apparatus is well shown in Figure 2. The ordinary manometer tube is replaced by a larger U-tube having a double scale for reading the height of the mercury column. Resting on the left mercury column is an ivory float, which by an extension rod of aluminum works up

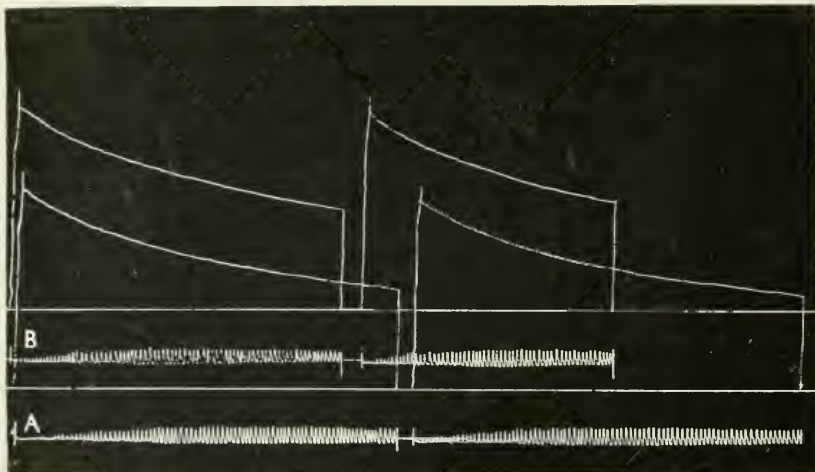


Fig. 3.—Graphic record made with Nicholson modification of Erlanger apparatus. *A*, record made with 13 cm. cuff; *B*, record made with 9 cm. cuff.

and down in a metal trough with a guide ring. At right angles to this extension is fastened an arm carrying a metal movable and adjustable needle, which comes in contact with the smoked paper of the revolving drum. In place of the glass bulb ordinarily supplied with the Erlanger apparatus, a much smaller bulb was substituted. This gives higher oscillations, as it reduces the amount of residual air between the rubber bulb and the interior of the glass bulb. The operation of the modified Erlanger apparatus is very simple. The recording portion of the instrument consists of two movable arms, one directly connected with the mercury float, which indicates on the drum the height of the mercury column. The other arm is activated by a rubber diaphragm, as in the original Erlanger apparatus, and

marks on the drum the oscillation of the blood in the artery under observation. The recording points of the movable arms are so adjusted that they are in the same vertical line. The arm attached to the mercury float is placed in contact with the smoked drum. The drum is then rotated one complete turn and thus indicates by a base-line the zero point of the mercury column. The lower arm is swung into position against the drum, and the apparatus operated as in the original Erlanger. The upper indicator records the height of the mercury column and the lower one shows the pulsation of the artery. The pressure is allowed to fall and the drum kept revolving, until the oscillations of the lower indicator have reached and passed their maxima, and are permanently lower. A glance at the record will help to make clear the operation of the modified apparatus (Fig. 3). The interpretation of the record is made as suggested by Erlanger. The point where the first abrupt increase in the size of the oscillations

TABLE 2.—PULSE-PRESSURE IN CHILDREN, VARIOUS OBSERVERS

Observers	Years													
	3	4	5	6	7	8	9	10	11	12	13	14	15	
M. Leitão	26.0	28.0	28.0	
W. Kriss	6.0	7.0	7.0	8.0	8.0	2.0	2.0	8.0	8.0	4.0	4.0	5.0	5.0	
W. Kaupé	8.2	8.1	8.2	15.4	13.0	10.3	8.5	15.1	8.8	8.9	8.6	11.0	
A. Katzenberger.	39.0	40.5	29.0	48.0	42.0	34.1	21.0	40.0	37.5	48.0	
Judson-Nicholson	26.2	26.7	26.9	25.3	26.9	28.9	23.3	32.1	31.5	37.1	33.1	38.7	38.1	

occurs, or where there is a characteristic drop in the base-line, is taken as the systolic pressure. The figures in millimeters of mercury are obtained by applying a millimeter rule at right angles to the lower curve, and measuring the distance from the point where the rule bisects the base line of the upper curve to the curve proper, then doubling the figures obtained. The doubling of the figures is necessary to allow for the depression of one arm of the mercury column in the U-tube, while the other is being elevated. The diastolic pressure is obtained by determining the point where the pulsations begin to diminish in height, and by measuring from the base-line to the corresponding point in the upper curve. In certain cases the oscillatory curve reaches its maximum height, then gradually diminishes, only to rise again to a second maximum of oscillation, following which is a gradual and continuous lowering of the oscillations.

We have followed Dr. Erlanger's interpretation and used the second maximum oscillation as designating the correct diastolic pres-

sure. This method gives a permanent record which is rapidly and accurately taken and eliminates the long time necessary, when the intermittent method of determining the diastolic pressure is used* (as recommended by Dr. Erlanger).

In conducting our investigations we have used readings taken by three main methods, auscultation, oscillation with the pith-ball apparatus and the modified Erlanger apparatus. All readings were taken between meals with the children in a reclining position, and the children rested between readings. In all cases we used the largest cuff available in proportion to the arm and a smaller cuff for comparative results. The children ranged from 3 to 15 years and were in daily

TABLE 3.—BLOOD-PRESSURE—

Observers	Method	Cuff cm.	Age, Years									
			3		4		5		6		7	
			Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.
L. Gordon	Palpation	12	81.0	83.0	86.5	88.5	85.0
Stowell	Palpation	12	91.0	89.0	95.0	96.0	102.0
Leitão	Erlanger	6	91.0	65.0	99.0	71.0	99.0	71.0
Kaupe	Palpation	12	90.0	81.8	86.4	78.3	82.2	74.0	97.5	82.1	91.0	78.0
W. Kriss	Auscultation	5	80.0	74.0	83.0	76.0	83.0	76.0	90.0	82.0	90.0	82.0
	Dias. 5 Phas.											
Katzen- berger	Auscultation	9.5	93.0	54.0	94.5	54.0	82.0	53.0
	Dias. 5 Phas.											
Judson and Nicholson	Modified Erlanger	13 and 9	91.8	65.6	91.6	64.9	91.3	64.4	92.6	67.3	94.0	66.3

attendance at the public schools, residing at the Foster Home and the Southern Home. Most of these children were well nourished and in good physical condition, and a number of them were above the average in development. After school hours, they were occupied with outdoor sports and games, for which there were ample facilities. We consider them representative of the average child.

Our studies started one year and a half ago and cover some two thousand three hundred observations. In a large number of cases we took readings by the auscultation method, while the records were being made on the drum of the modified Erlanger apparatus, so that they afford a very good means of comparison of the two methods. We believe that we have established a standard of blood-pressure in the normal child between the ages of 3 and 15 years. The results obtained with the modified Erlanger apparatus we have taken as the standard.

That they are correct becomes apparent when we consider the uniformity of the readings for the systolic and diastolic pressures. Comparison of the results obtained by the conjoint use of the auscultation and modified Erlanger methods further confirms their accuracy. The method of recording the results on the modified Erlanger apparatus thoroughly eliminates the personal equation, as both the oscillatory curve produced by the pulse-wave and the height of the mercury column are recorded automatically on the moving drum. The finished records can be studied and accurately interpreted at our leisure, determination of the systolic and diastolic pressure being easily obtained by careful measurements of the curve.

—IN NORMAL CHILDREN

Age, Years															
8		9		10		11		12		13		14		15	
Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.
93.0	100.0	95.0	104.0	105.0	107.0	110.0	109.0
101.0	102.0	112.0	102.0	111.0	107.0	110.0	109.0
.....
90.5	80.2	90.0	81.5	97.7	82.6	96.0	87.2	92.0	83.1	96.6	88.0	107.0	96.0
90.	88.0	90.0	88.0	98.0	90.0	98.0	90.0	99.0	95.0	99.0	95.0	101.0	96.0	101.0	96.0
103.0	55.0	100.6	58.6	104.6	69.5	99.8	78.8	108.2	68.2	107.7	70.2	119.2	71.2
93.6	64.7	94.3	71.0	99.2	67.1	97.1	65.5	102.3	65.2	103.6	70.5	106.1	67.4	105.6	67.5

The criticism may be made that, while the table represents the summary of a large number of observations, the individual variations might still be so considerable as to impair its value. We find that the widest variations occur from the tenth to the fourteenth year when there is a marked rise in the systolic pressure. From the fourth to the fourteenth year, inclusive, the variations do not exceed 5 mm. in two-thirds of our cases, and in three-fourths of them, the blood-pressure shows a variation of less than 8 mm.

The systolic pressure shows a slight but gradual rise from 3 to 10 years. From 10 to 14 years the increase is more abrupt, with a rapid elevation in the fourteenth year during adolescence. The systolic pressure varies from 91 mm. in the fourth year to 105.5 mm. in the fourteenth year.

Our results show that the systolic pressure is higher than that generally accepted and does not show any arithmetical increase from year to year. The total rise in systolic pressure from 4 to 14 years is represented by only 14 mm. of mercury.

In contrast to the systolic pressure, the diastolic remains at an almost uniform level, and the pulse-pressure increases progressively and proportionately more than the systolic pressure over the corresponding period. Comparing the systolic pressure at 4 years with that of 14 years, we find an increase of 16 per cent., whereas the increase in the pulse-pressure during the same period amounts to 45 per cent.

Comparing the results obtained by using cuffs of different width, we find that from 4 to 8 years the circumference of the arm varies from 13 to 18 cm., and that the 9-cm. cuff gives as accurate results as when wider ones are used (11 to 13 cm.). From 8 to 15 years the circumference of the arm varies from 14 to 25 cm. During this period we find more accurate results when using the 13-cm. cuff. Concerning the influence of the pulse rate, we believe that the large number of observations taken on the same child practically eliminates errors due to this cause.

Comparison of the results obtained by the auscultation method with those of the modified Erlanger method, show remarkable uniformity in the readings. The auscultation method requires no complicated apparatus, is easily carried out, and gives accurate results if the necessary precautions are taken to observe correct technic, especially as to the mode of application and width of the cuff.

In comparing the results of the auscultation with other methods, we find the average variation in the systolic pressure ranged from 1 mm. more to 6.5 mm. less than the readings obtained when using the modified Erlanger apparatus.

The diastolic readings on the other hand, were from 1 to 5 mm. lower, except at 9 years and 13 years when they were respectively 9 and 7 mm. lower, the result is a higher pulse-pressure averaging 4 mm. for the period covered in our tables.

On reviewing the results obtained by the pith-ball method, we find the systolic pressure ranges from 7 mm. above to 1 mm. below the readings of the modified Erlanger. The diastolic pressure varies from 2 mm. above to 5 mm. below, with the exception of the eighth year, when it was 8 mm. above the figure on the modified Erlanger instrument. This produces an average increase of 1.5 mm. in the pulse-pressure.

When we use the auscultation method in children, we must take the time of appearance of the dull sound (fourth phase) as the time

to read the height of the mercury column, which gives the correct diastolic pressure. If the time of disappearance of all sound (fifth phase) is taken, the error varies from 11 to 20 mm. This makes a very marked difference in the pulse-pressure.

The results obtained with the pith-ball apparatus compare favorably with those obtained by the other two methods. In our table the figures given for children aged 3 years and 15 years, were not utilized in drawing conclusions, as the number of observations was too small.

In closing we must insist on the importance of repeated observations in a given case before reaching conclusions. The figures in our tables represent the averages of a large number of readings; we do not claim that they are an *absolute* standard. While in the individual child the variations in the systolic pressure may be considerable, diastolic pressure remains fairly constant. The importance of determining the diastolic pressure in every case cannot be too strongly emphasized. The determination of the pulse-pressure, indicating as it does the peripheral resistance, is the most important point to be determined in children.

A STUDY OF THE BLOOD-PRESSURE IN ANEMIA IN INFANCY *

JOHN LOVETT MORSE, A.M., M.D.

Associate Professor of Pediatrics, Harvard Medical School

AND

EDWIN T. WYMAN, M.D.

Assistant Physician at the Children's Hospital

BOSTON

This study was undertaken because of the unexpected results obtained in an examination of the blood-pressure in a marked case of anemia in an infant. The history of this case will be given in detail further on. It was found on looking up the literature that there were very few data as to the blood-pressure in infancy, whether in health or in disease, and practically nothing as to the blood-pressure in anemia in infancy.

Shaw,¹ using Gärtner's tonometer, made 400 measurements on forty-five children ranging in age from 3 months to 12 years. He found that the systolic pressure under normal conditions varied between 90 and 110 mm. He also found that the age of the child appeared to have very little influence on the height of the blood-pressure.

Cook and Briggs² found that the systolic pressure during the first two years varied between 75 and 90 mm. They used a modification of the Riva-Rocci instrument and determined the pressure by palpation. They do not state the width of the band used, and give no data as to the number of babies examined.

Beretta³ found that the systolic pressure in babies during the first year varied between 54 and 87 mm., the average being 76 mm. He used the Riva-Rocci instrument.

Stone⁴ found that the ordinary reading in infants under 6 months was between 60 and 70 mm., and between 2 and 3 years, 80 to 90 mm. He used the Riva-Rocci apparatus, but gives no data as to

* From the Medical Service of the Children's Hospital, Boston.

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

1. Shaw: Albany Med. Ann., 1900, xxi, 88.

2. Cook and Briggs: Johns Hopkins Hosp. Rep., 1903, xi, 451.

3. Beretta: Abstr. in Monatschr. f. Kinderheilk., 1903-4, ii, 725.

4. Stone: Boston Med. and Surg. Jour., 1904, cl, 262.

the width of the cuff used, where the pressure was taken or how many babies were examined.

Oppenheimer and Bauchwitz⁵ examined sixty-eight children ranging from the new-born to 14 years of age. They do not give the number of children tested at the different ages. They used a modification of the Riva-Rocci instrument, with a cuff 5 cm. in width. They state that the blood-pressure between birth and 6 months is 80 mm., from 7 months to 1 year, 90 mm., and from 2 years to 3 years, 90 mm.

Trumpp⁶ made 1,062 observations on fifty-six infants, using Gärtner's tonometer. He found that the systolic pressure in healthy, quiet infants varied between 60 and 90 mm., the average being 80 mm. Readings between 60 and 70 mm. were ordinarily found only during sleep or in premature or feeble infants. The pressure was the same in the new-born as in older infants. Nervous excitement and muscular activity increased the pressure from 10 to 60 mm. The taking of food increased it from 8 to 10 mm. He studied nine cases of acute and eight of chronic disturbances of nutrition and found that the blood-pressure sank with the increase in the debility. Anything under 50 mm. was a bad sign. When there were marked changes in weight, the blood-pressure rose and fell with the weight. The blood-pressure rose with water retention.

Gordon⁷ studied 170 normal children, but does not state the number of children at the various ages. He used Martin's modification of the Riva-Rocci instrument, with a cuff 12 cm. in width. He found that the systolic pressure under 1 year was 71 mm., at 1 year, 73 mm., and at 2 years 79.5 mm. He states that the figures are higher if a narrower armlet is used.

Hill⁸ made nineteen examinations on sixteen babies under 2 years of age, ill with gastro-enteritis. The average systolic pressure in these cases was 102 mm., the average diastolic, 81 mm., and the average pulse-pressure, 21 mm. The highest systolic pressure was 130, the lowest, 85; the highest diastolic, 118, and the lowest, 60; the highest pulse-pressure 36 and the lowest 8. He emphasizes the importance of the pulse-pressure, and says that it is far more important than the systolic pressure alone. The pulse-pressure was somewhat lower in the infants that died, but there were many exceptions. He concludes that the blood-pressure is not of the same importance in infants as in adults. He used the Nicholson sphygmomanometer, a modification of the Riva-Rocci type. The instrument was applied on the

5. Oppenheimer and Bauchwitz: *Arch. f. Kinderheilk.*, 1905, xlii, 415.

6. Trumpp: *Jahrb. f. Kinderh.*, 1906, lxiii, 43.

7. Gordon: *Arch. Pediat.*, 1911, xxviii, 343.

8. Hill: *Arch. Pediat.*, 1913, xxx, 588.

TABLE 1.—NORMAL INFANTS

No.	Age in Months	Sex*	Systolic Pressure	Diastolic Pressure	Pulse Pressure	Hemo-globin %
1	2	♀	80-76	50-57	30-19	70
2	2½	♀	72	58	14	
3	3	♂	84	62	22	
4	3	♂	78	65	23	
5	3	♀	100-97	70-74	30-23	75
6	3	♂	78	64	14	
7	3	♂	78	61	17	
8	4	♂	82	69	13	
9	4	♂	88-90	52-57	36-33	80
10	4½	♂	80-92	44-60	36-32	
11	5	♂	82	64	18	
12	6	♂	92-96	75-74	17-22	
13	6	♂	98	82	16	80
14	6	♂	88	72	16	
15	6	♀	94-95	40-60	54-35	
16	6	♀	86	67	19	
17	6	♂	84-87	44-56	40-31	80
18	6½	♂	98	78	20	
19	7	♀	90-92	50-57	40-35	
20	7	♀	90	76	14	
21	8	♀	86	63	23	80
22	8	♂	83	74	9	
23	8	♀	95	64	31	
24	8	♂	80-94	40-52	40-42	
25	8	♀	110	80	30	80
26	8	♂	88	59	29	
27	8½	♂	80-92	45-56	35-36	
28	8½	♂	95	70	25	
29	9	♀	87	68	19	70
30	9	♂	110	80	30	
31	10	♂	102-100	76-80	26-20	
32	10	♂	87	72	15	
33	11	♂	85	60	25	80
34	11	♀	82	69	13	
35	11	♀	82	59	23	
36	11	♂	89	66	23	
37	11	♀	92	78	14	80
38	11	♀	100	76	24	
39	12	♂	94-92	70-73	24-19	
40	12	♂	100	74	26	
41	12	♀	95	65	30	80
42	12	♂	90	75	15	
43	12	♀	92	60	32	
44	13	♂	98	76	22	
45	13	♀	92	60	32	80
46	14	♂	100	80	20	
47	14	♂	97	83	14	
48	15	♂	100	79	21	
49	17	♂	100	70	30	80
50	22	♂	104	84	20	
Average			90	66	25	

* In this and the following tables ♂ stands for male and ♀ for female.

thigh and the readings made by auscultation over the popliteal artery. The systolic pressure was measured from the first sound heard, and the point at which the sound entirely disappeared was taken as the diastolic pressure.

It seemed advisable, therefore, to examine first a series of normal infants, in order to get a more definite normal standard. A series of poorly nourished babies, not suffering from anemia, was then examined to determine what effect, if any, the condition of the nutrition had on the blood-pressure. A small series of babies suffering from moderate anemia was then examined, and finally, a more detailed examination of the baby suffering from severe anemia was made.

The "Tycos" sphygmomanometer was used in this study. The width of the band was 5 cm. The tests were made on the arm, when possible, otherwise on the thigh. As a matter of fact, about one-half of them were made on the arm and one-half on the thigh. The determinations of the blood-pressure were all made with the stethoscope, the bell being applied over the vessels at the elbow when the cuff was applied on the upper arm, and in the popliteal space, when it was applied on the thigh. The systolic pressure was read when the sound was first heard; the diastolic pressure was read when the sound changed from sharp to dull.

Sixty-two observations were made on fifty normal babies. These results are given in detail in Table 1. The average systolic pressure in normal babies under 2 years of age was, therefore, 90 mm., the average diastolic, 66 mm., and the average pulse-pressure 25 mm.

TABLE 2.—COMPARISON BETWEEN VARIOUS PRESSURES IN THE FIRST AND SECOND YEARS

	First Year	Second Year
Number of Cases.....	38	12
Average Systolic Pressure	89	95
Average Diastolic Pressure	64	73
Average Pulse-Pressure	25	24
Highest Systolic Pressure.....	110	104
Lowest Systolic Pressure.....	72	90
Highest Diastolic Pressure.....	82	84
Lowest Diastolic Pressure.....	40	60
Highest Pulse-Pressure	54	32
Lowest Pulse-Pressure	9	14

Thirty-two of these babies were males and eighteen females. The average systolic pressure in the males was 91 mm. and in the females 86 mm. The average diastolic pressure in the males was 68 mm. and in the females, 64 mm. The average pulse-pressure in the males was

TABLE 3.—POORLY NOURISHED INFANTS

No.	Age in Months	Sex	Systolic Pressure	Diastolic Pressure	Pulse-Pressure	Hemo- globin Red Corpuscles	Diagnosis	General Condition	Spleen
1	1½	♂	74	36	38	80%	Indigestion, malnutrition	Poor	
2	2	♂	74	45	29		Pyloric spasm	Poor	
3	2	♀	69	40	29		Pyloric spasm	Poor	
4	2	♀	72	43	29		Feeding	Poor	
5	2½	♀	64	40	24	70%	Malnutrition	Fair	
6	3	♀	72	46	26		Malnutrition	Poor	
7	3	♀	60	47	13		Pyloric spasm	Poor	
8	3	♀	75	40	35		Indigestion	Poor	
9	4	♀	80	50	30		Feeding	Good	
10	4	♀	84	57	27		Pyloric spasm	Poor	
11	5	♀	80	40	40		Feeding	Fair	
12	5	♀	93	54	39		Indigestion	Fair	
13	5	♀	60	40	20		Malnutrition	Poor	
14	5	♀	83	52	31		Malnutrition	Poor	
15	7	♂	70	30	40	80%	Rachitis	Fair	Spleen +
16	7	♂	75	30	45	4,000,000			
			92	35	57	70%			
			90	40	50	4,550,000	Malnutrition	Good	Spleen +
17	7	♀	94	63	31		Feeding	Poor	
18	10	♂	92	51	41		Syphilis	Poor	
19	10	♀	90	45	45		Scorbutus	Fair	
20	11	♀	87	60	27		Pyloric spasm	Poor	
21	11	♂	100	65	35		Malnutrition	Fair	
22	12	♀	90	72	18		Malnutrition	Fair	
23	13	♂	106	68	38		Malnutrition	Poor	
24	15	♂	102	73	29	80%	Otitis media	Poor	
						60%			
25	19	♂	87	60	27	6,480,000	Rachitis	Fair	
Average	89	53	36				

25 mm. and in the females, 27 mm. These differences are so slight that they are presumably unimportant. They do show, however, a slightly higher pressure, in both systole and diastole, in the males than in the females.

The highest systolic pressure was 110, and the lowest 72 mm., while the highest diastolic was 84, and the lowest diastolic 40 mm. The pulse pressure varied between 54 mm. and 9 mm.

TABLE 4.—ANEMIC INFANTS

Number	Red Cor- puscles	Hb., %	Spleen	Age in Months	Sex	Systolic Pressure	Diastolic Pressure	Pulse-Pressure	Murmur in Neck	Murmur in Heart	Murmur in Groin	Pistol Shot
1	2,000,000	40	Palpable at navel	4	♂	114	42	72	Systolic	Systolic at base	0	0
2	2,400,000		0	12	♂	120	40	80	Systolic	Systolic over whole precordia	Systolic	0
	2,600,000	30	♂	95	60	35	Systolic	Systolic over whole precordia	Systolic	0
	2,640,000	31	♂	120	55	65	Systolic	Systolic over whole precordia	Systolic	0
3	3,000,000	60	2 cm.	4	♂	100	20	80	Systolic	Systolic	0	0
4	3,200,000	70	Enlarged	8	♀	100	45	55	Systolic	Systolic	0	0
						105	45	60				
5	3,496,000	65	Just Palp- able	2	♂	60	25	35	0	0	0	0
						65	29	36				
6	3,500,000	70	0	3½	♂	90	40	50	Systolic	0	0	0
7	3,744,000	65	0	10	♂	96	40	56	0	0	Systolic	0
8	3,800,000	80	0	4	♂	84	48	36	0	0	0	0
9	3,800,000	75	0	8	♂	105	53	52	Systolic	0	0	0
10	4,000,000	50	0	8	♂	100	35	65	0	0	Systolic	0
						110	35	75				
	Average				97	41	57				

Table 2 gives a comparison between the various pressures in the first year and in the second year. These figures seem to show that both the systolic and the diastolic pressure are somewhat higher during the second than during the first year, while the pulse-pressure is the same. The number of cases is too small, however, to warrant very definite conclusions on these points.

Twenty-seven observations were made on twenty-five poorly nourished, but not anemic, babies. These results are given in detail in Table 3.

The average systolic pressure in these babies was, therefore, 89 mm., the average diastolic, 53 mm., and the average pulse-pressure, 36 mm. The highest systolic pressure was 106 mm., and the lowest 60 mm., while the highest diastolic pressure was 73 mm. and the lowest diastolic pressure 30 mm. The highest pulse-pressure was 57 mm. and the lowest 13 mm. Comparison of the blood-pressures in the normal and poorly nourished babies shows that, while the average systolic pressure was practically the same in both cases, the diastolic pressure was lower and the pulse-pressure, therefore, higher in the poorly nourished babies.

Fifteen observations were made on ten babies suffering from anemia. These cases have been arranged in Table 4 according to the number of red corpuscles and not according to the age. This table shows that the systolic pressure was somewhat higher in these babies than in either the normal or the poorly nourished babies, while

TABLE 5.—

Age in Months	Hb., Per cent.	Red Corpuscles	White Corpuscles	Spleen, cm.	Liver, cm.	Systolic Pressure
12	25	1,800,000	28,000	5	2	124
14	55	2,720,000	47,000	6	4	100
18	70	3,776,000	?	4	4	110
24	?	?	?	13	5	120
25	40	2,480,000	19,500	13	5	124

the diastolic pressure was considerably lower and the pulse pressure, therefore, much higher. There was no definite relation, however, between the amount of the pulse-pressure and the degree of the anemia.

The most interesting observations were those in the baby suffering with severe anemia, to which reference has already been made. This baby was 12 months old when first seen. He was markedly pale, but not badly nourished. The left border of the heart was 6 cm. to the left, and the right border 2.25 cm. to the right of the median line, while the upper border was at the upper border of the third rib. The first sound over the whole precordia was followed by a blowing murmur, loudest in the third left interspace. It was transmitted better to the left axilla than to the right. The second pulmonic was considerably louder than the second aortic sound. There was no thrill. There was a pistol-shot in the groin. There was also a systolic murmur, but no diastolic murmur, in the groin. There was

a Corrigan as well as a capillary pulse. The extremities were not clubbed. The lower border of the liver was 2 cm. below the costal border in the nipple line, while the lower border of the spleen was 5 cm. below the costal border. The hemoglobin, estimated with the Sahli apparatus, was 25 per cent. There were 1,800,000 red corpuscles and 28,000 white corpuscles. The red corpuscles showed marked variation in size and shape, with marked polychromatophilia. There were many stippled cells. Thirteen normoblasts were seen in counting 100 white cells. A differential count showed: mononuclears, 44 per cent.; transitional forms, 12 per cent.; polynuclear neutrophils, 39 per cent.; eosinophils, 5 per cent.

The systolic blood-pressure was 124, and the diastolic pressure 0, giving a pulse-pressure of 124 mm. That is to say, the conditions in the peripheral circulation corresponded exactly to those found in aortic regurgitation in adults. It was thought for a time that there

—SEVERE ANEMIA

Diastolic Pressure	Pulse-Pressure	Murmur in Heart	Bruit in Neck	Murmur in Groin	Pistol Shot
0	124	Systolic over whole precordia	Systolic	Systolic	+
15	85	Murmur less marked.	Systolic	Systolic	0
30	80	Very slight systolic at base	Systolic	0	0
0	120	Systolic at base	Systolic	Systolic	+
30	94	Systolic at base	Systolic	0	0

must be an aortic regurgitation. Then the query arose as to whether these conditions might not be due to some change in the peripheral circulation as the result of the severe anemia. Further observations on the baby, which are detailed in Table 5, show that the latter was the true explanation.

When he was last seen, when 25 months old, he was fairly developed and nourished, but still markedly pale. He showed many of the changes in the bones characteristic of rickets. His heart was of normal size. There was a systolic murmur at the base of the heart, loudest in the pulmonic area. It was also audible along the sternum to the fourth left space. There was a bruit in the neck. There was a systolic murmur in the groin, but no pistol-shot. The liver was palpable 5 cm. below the costal border in the nipple line. The spleen filled the whole left half of the abdomen, extending 3 cm. beyond the median line.

The examination of the blood gave the following results:

Hemoglobin	40 per cent. (Sahli)
Red corpuscles	2,480,000
White corpuscles	19,500
Small mononuclears	28 per cent.
Large mononuclears and transition forms.....	76 per cent.
Polynuclear neutrophils	6 per cent.
Eosinophils	0 per cent.

The red corpuscles showed marked achromia and there was considerable variation in their size and shape, as well as polychromatophilia and basic stippling. Eight normoblasts and one megaloblast were seen while counting 200 white cells.

Comparison of the observations in this instance with those in the other anemic babies, the poorly nourished babies and the normal babies, show that with disturbances of nutrition there is a progressive lowering of the diastolic pressure and a corresponding increase in the pulse pressure. The systolic pressure, on the other hand, rises with the increase of the anemia. These observations merely bring out certain facts but, unfortunately, do not warrant any definite conclusions as to their cause.

70 Bay State Road—483 Beacon Street.

FURTHER ANALYSIS OF THE VOICE SIGN IN CHOREA *

WALTER B. SWIFT, M.D.

BOSTON

Elsewhere¹ I have reported in a short preliminary note on the voice in chorea as analyzed by the aid of the vocal kymograph. This was merely the first blush, the original snap-shot of a single isolated case.

That note briefly reviewed the literature since 1841, showed the vagueness of former descriptions of choreic vocal changes, the antiquated methods of vocal analysis, the advantages of modern methods, and finally presented — as far as I know — the first clear statement of just what choreic voice is. Without reiterating at length the details of that preliminary note, let me briefly state that the voice-change as reported on the kymograph consists in a variation in two vocal elements — a rise in pitch and an increase in intensity. This vocal change was so constant and so uniformly simultaneous with other choreiform movements that I there presented the claim that these vocal changes deserved at least to be classed with Shaw's² knee-jerk in chorea and with Graves'³ respiratory signs in chorea, and should therefore in routine clinical examination be called the voice sign in chorea.

From the start I felt that the preliminary note should be followed up by a variety of tests carried uniformly through a long series of cases in order to ascertain the varieties of the voice sign in different aspects of the disease — early, marked, late, recovered, partial and hemichorea — as well as to ascertain if change in pitch and vocal intensity were the only effects of choreic movements on vocal utterance; also the varieties of these in different stages and forms if any.

It is the procedures and results of this research that I now present. Let me here express my appreciation to Prof. John J. Thomas for opportunity to carry on this investigation.

* Read before the Section on Nervous and Mental Diseases at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

* From the Neurological Department of Boston City Hospital, Service of Prof. John Jenks Thomas.

1. Swift, Walter B.: A Voice Sign in Choreia: Preliminary Note, *AM. JOUR. DIS. CHILD.*, June, 1914, p. 422.

2. Shaw, H. L. K.: The Knee-Jerk in Choreia, *Albany Med. Ann.*, May, 1897.

3. Graves, W. W.: A Study of the Respiratory Signs of Choreia Minor, *The Journal A. M. A.*, Jan. 30, 1909, p. 364.

In conversation, vocal changes are short in duration, and hence difficult of perception. This suggested the prolongation of tests to make vocal change more easily perceived. The change recorded from prolonged tests must necessarily be the same changes elongated that occur in conversation, where the sounds are short.

Twenty cases were then subjected to the following series of twenty-seven tests, 540 tests in all:

1. Prolonged utterance of a as in arm.
2. Prolonged utterance of e as in eye.
3. Prolonged utterance of i as in ice.
4. Prolonged utterance of o as in old.
5. Prolonged utterance of u as in rude.
6. Prolonged utterance of a as in ask.
7. Prolonged utterance of e as in end.
8. Prolonged utterance of i as in ill.
9. Prolonged utterance of o as in odd.
10. Prolonged utterance of u as in up.
11. Consonant p.
12. Consonant b.
13. Consonant m.
14. Consonant t.
15. Consonant d.
16. Consonant n.
17. Consonant k.
18. Consonant g.
19. Consonant r.
20. Consonant l.
21. Consonant s.
22. Prolonged whisper.
23. Prolonged whistle.
24. Blowing the breath.
25. Holding the breath in inspiration.
26. Holding the breath in expiration.
27. Holding the breath in half expiration.

The purpose in trying so many tests was to expose all the forms and modes of vocal production to the choreic twitch, and in this way ascertain the mode and form acted on with highest frequency to serve as a single test adapted to routine clinical examination.

SYMPTOM FREQUENCY IN TWENTY CASES

After tabulating 20 cases of supposed chorea, 4 were found recovered, and 1 a question of hysteria. Excluding those 5, 15 are left, of certain diagnosis on which to base results.

In general, variation in pitch and intensity occurred in two-thirds of the cases pretty uniformly distributed over all the vowel sounds, long and short, with a slightly more frequent change in pitch than intensity. Therefore I place pitch first in mentioning them. There is, however, one marked difference in all these vowel changes. Long "a" is more marked in its change. This is a good reason for its choice

as the routine clinical test. The explanation may lie in the open position of vocal agents in the utterance of "a" long, as in "are," thus allowing any contraction to show more in its effect, than if exerted on a closed position of those agents as "e" in "end."

The whisper changed in pitch in 3 cases, in intensity in 6, showing periodic cessation in 3. The whistle showed irregularity in 3 on expiration, and in 3 cases on inspiration. One case entirely stopped whistling. Three cases could never whistle. One showed periodic cessation of tones, with no change in pitch or intensity determinable.

Consonants showed no change except when prolonged, where three cases showed "e" and "r" to change in pitch and intensity.

Air blow: 4 cases were irregular; 3 halting.

Air held in inspiration, no change.

Air held in expiration showed one puff.

Air held in half expiration showed one puff.

OTHER SIDE OBSERVATIONS NOTED IN THE 540 TESTS OF TWENTY CASES

Cases recovered in from three to five months showing no voice sign.

Also one case recovered in eight months showed no voice sign.

The frequency of occurrence slightly increased with the increase of fatigue.

Once was observed a nasal puff of air, simultaneous with a choreic twitch, mouth closed.

One relapsed case with motions in limbs only showed no voice sign whatever.

One case hemichorea showed vocal changes, like the others.

One case with a uniform and constant vowel variation in pitch and intensity, and that, too, in all the vowels tested showed no vocal change in prolonged "l" and "r."

Voice changes not always in proportion to the amount of choreic motion as seen.

With air held in inspiration, expiration and half expiration, slight movements showed no change in 8 cases.

Marked timidity and slight questionable voice changes should not be counted as positive change.

Slight lack of articulation control or inattention may contribute slight negligible voice changes.

Marked contractions accompany marked voice change.

CONCLUSIONS FROM TWENTY CASES

1. These choreic voice changes are more frequent in the vowels, less so in whisper, whistle, consonants, air blow and holding of breath; and are less and less in frequency in this order.

2. There is sufficient uniformity and frequency in the appearance of vocal changes to warrant us in classifying changes of pitch and intensity as one of the signs of chorea; of equal dignity with the choreic knee-jerk of Shaw,² the respiratory signs of Graves³ and other minor symptoms.

3. Other less frequent and less marked changes occur that seem of interest subordinate to those in the vowels.

4. The most marked change occurred in the open prolonged sound of "a" as in "are," and I therefore offer this as the routine clinical test and method for the elicitation of the choreic voice sign.

SUMMARY

Analysis of twenty cases of chorea with over five hundred observations on the voice show a change of pitch and intensity in two cases out of three—a change that deserves recognition as a new sign in chorea—the choreic voice sign.

110 Bay State Road.

THE DIAGNOSIS AND TREATMENT OF "LATE" HEREDITARY SYPHILIS *

BORDEN S. VEEDER, M.D., AND P. C. JEANS, M.D.
ST. LOUIS

RELATION OF "EARLY" TO "LATE" SYPHILIS

During the past two years we have seen 123 cases of manifest hereditary syphilis at the St. Louis Children's Hospital. Of these seventy-four, or 60 per cent., belonged to the group commonly described as "late" hereditary syphilis while only forty-nine, or 40 per cent., were infants under 1 year of age with the classical symptoms of rash, coryza, and enlarged spleen which characterize the "early" type. The division into "early" and "late" is arbitrary and only a matter of convenience, as these "early" symptoms may first develop after infancy, while "late" lesions may develop early in infancy. The "late" lesions may also develop primarily in older children without any "early" lesion having occurred or been recognized. Thus lesions comparable with the secondary (eruptive), tertiary (gummatous), and quarternary or para-syphilitic (vascular and nervous lesions), stages of acquired syphilis, are included among the clinical manifestations of "late" hereditary lues.

In only twelve of our cases were we able to obtain a positive history of an "early" lesion in infancy, while in twenty-five cases the history was definitely negative in regard to this point. In the remainder the history was indefinite or could not be obtained. It is highly probable that some of our forty-nine "early" cases will later develop other symptoms and thus ultimately belong to the group under consideration. In connection with the large group of cases without early lesions it is interesting to note a study¹ of the Wassermann reaction in 101 infants in St. Louis (thirty-three of whom were from this clinic) who showed no clinical evidences of syphilis. But two positive and one doubtful reactions were obtained. Although this series is small, it would tend to show that the latent infections in infancy are not so extremely common in St. Louis as might be imagined from our figures.

* Submitted for publication, June 17, 1914.

* From the Department of Pediatrics, Washington University Medical School and the St. Louis Children's Hospital.

* Read at the annual meeting of the American Pediatric Society. Stockbridge, Mass., May 28, 1914.

1. Blackfan, Nicholson and White: AM. JOUR. DIS. CHILD., 1913, vi, 162.

We are now making a study of latent infection in older children by testing the blood and examining the brothers and sisters of the patients in our series. A large percentage of such children have given positive Wassermann reactions although they have never shown clinical evidences of luetic infection. Many items of interest have occurred in these familial studies which will be reported later.

GENERAL STATISTICS

The ages of the seventy-four patients were as follows:

Years of age.....	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12
No. of cases.....	6	4	6	4	6	4	10	7	5	5	11
Years of age.....	12-13	13-14	14								
No. of cases.....	2	2	2								

Eighty-three per cent. of the patients were white and 17 per cent. colored, while of the total clinic attendance 92 per cent. are white and 8 per cent. colored. Thirty-three were males and forty-one were females.

We were able to obtain a definite history of the feeding in infancy in twenty-seven cases. Twenty-three had been breast-fed and only four artificially fed. This may be looked on as an illustration of the better chances for life of the breast-fed syphilitic infant over the artificially fed, as the ratio is much different from the ratio of the breast to bottle-fed infants in general.

CLINICAL LESIONS

The following list of clinical diagnoses shows the wide variety of lesions encountered. In many cases there were multiple lesions, and the following figures give the number of cases in which each lesion occurred. In every case there was a positive Wassermann reaction which was checked in practically every instance by a second test.

Bones—		Central nervous system †—	
Periostitis tibia	3	Mental deficiency	14
Periostitis skull	1	Cerebrospinal syphilis	8
Joints—		Hemiplegia	5
Acute arthritis knee	7	Epilepsy	4
Acute arthritis ankle	1	Paralysis	3
Skin—		Chorea	2
Macular eruption	1	Hydrocephalus	2
Alopecia	2	Ulcerations—	
Condyloma anus	3	Nasal	2
Gummata	3	Laryngeal	1
Eye—		Pharyngeal	1
Interstitial keratitis	17*	Ozena	1
Choroiditis	1	Enlarged spleen (only lesion)...	1
		Torticollis	1
		Aortitis	1
		Obscure abdominal pain.....	1
		Obscure pain in legs.....	2

* 23 per cent.

† Thirty-two patients in all or 43 per cent.

The large number (43 per cent.) of our patients with lesions of the central nervous symptoms is one of the most interesting features from the standpoint of diagnosis. During the past two years we have tested the blood of thirteen patients with hemiplegia admitted to the wards of the hospital of which five reacted positively. In one case—a girl of 5 years—admitted at the onset of the trouble, we were able to limit the extent of the lesion by a vigorous treatment. Some of these cases had been previously looked on as poliomyelitis. Two of the eight cases reacting negatively were unquestionably birth injuries. Of eight cases of chorea tested (following and including the first positive case whose history is given later), two gave positive Wassermann reactions. In three of the negative cases there was a definite history of rheumatism, while no history or evidence of rheumatism was noted in the two positive cases and in the three remaining negatively-reacting cases.

Mental deficiency was usually associated with some other condition as epilepsy or cerebrospinal syphilis. During the period covered by our cases there were thirty-three cases of mental deficiency admitted to the wards of the hospital of whom fourteen were syphilitic. This is a very much higher percentage than is usually found and does not express the true relation of mental deficiency due to syphilis to mental deficiency in general, but is the result of admitting cases for this particular study.

Among the more unusual lesions were an aotitis and a torticollis. Three patients with indefinite pain of obscure origin—once in the abdomen and twice in the legs—which had persisted irregularly for some time and for which no cause could be found, gave positive Wassermann reactions and the pain disappeared under specific treatment. The cases of acute arthritis were very interesting. Some patients were sent to us for tuberculosis and others for acute articular rheumatism. One case (knee) developed in a child with a tuberculous hip who had been under observation and treatment in the orthopedic department for several years.

The absence of Hutchinson's teeth which is so generally described as a common symptom of syphilis was very noticeable in our cases. In forty-eight patients who were old enough to have permanent incisors the teeth were notched in but three instances. Ill-shaped and deformed teeth were very common. They were usually small and peg-shaped with broken, irregular surfaces, and were separated widely from one another and without good alignment. We have also observed typical Hutchinson's teeth in a non-syphilitic patient.

It will be noted that most of our cases fall into one of three large groups. The first of these is made up of eye conditions (24 per

cent.) and is so well recognized that it needs no discussion. The second comprises lesions of the central nervous system (43 per cent.). So many of these cases have given positive Wassermann reactions when there has been nothing to suggest lues in the early or family history that we now make the test as a part of the routine examination of nervous cases. The third group is in many ways the most interesting as it contains a group of cases less frequently recognized as of a possible syphilitic origin. It is made up of cases of chorea, acute arthritis, torticollis, and obscure muscular pain—in other words clinical conditions which are often grouped together as “rheumatic”—and amounts to about 20 per cent. of our cases. It has long been recognized that these acute “rheumatic” conditions are the result of bacterial toxins, and our cases would indicate that syphilitic infection of an hereditary nature is one of the common causes of these cases developing in childhood. We have checked the diagnosis of these cases by repeated blood tests and by Wassermann reactions on the parents. The strongest proof that they are the result of syphilis and not an accidental association lies in the rapidity with which the lesions improve under antisyphilitic treatment.

TREATMENT

The treatment we have gradually evolved consists of a combination of neosalvarsan and mercury. We prefer neosalvarsan to salvarsan because of the simplicity of the technic, which is an essential factor in dealing with children. The neosalvarsan is dissolved in 1 c.c. of freshly distilled water for each decigram and injected intravenously into any available vein with an ordinary glass hypodermic syringe. The entire preparation of the drug and syringe and the administration can be accomplished in from twelve to fifteen minutes. We made a number of intramuscular injections earlier but soon gave them up because of the pain and discomfort to the patient and the objections of the parents. The dose of the neosalvarsan varies according to the age and clinical condition of the patient—as a whole we give larger doses than are usually advised and have had no unpleasant or bad results. At first the injections were followed in a few instances by nausea and vomiting which we are inclined to attribute to the use of a “sterile” water instead of a freshly distilled water, as we have not observed such sequelae in the last year and a half. Although it is claimed by competent observers that neosalvarsan is less effective than salvarsan, we prefer neosalvarsan because it is effective and fulfills certain essential requirements for use with children which salvarsan does not. For the mercurial part of the treatment we have come to use gray powder exclusively in the late cases and to a very large extent

in the early cases. For the treatment of acute lesions (eruptions, ulcers, arthritides, etc.) the neosalvarsan is far more effective than inunctions of mercury, while the gray powder gives very good results and can be given over longer periods of time with less disturbance than mercury in any other form. We have had no experience with the mercurial injections which are so effective in the acquired forms of syphilis, as intramuscular injections are not practical with children, at least in the class of patients that we are treating.

The course of treatment we use varies somewhat, but with the usual case presenting an acute lesion is in general as follows: Three or four intravenous injections of neosalvarsan are given with a gradually increasing dosage two or three days apart. Then mercury is started, with small doses, which are gradually increased until the patient is taking a fairly large dose. In a few weeks this is interrupted for a short time and then repeated. In a number of cases a second and a third series of neosalvarsan injections are given alternating with the mercury. The mercurial treatment is continued for an indefinite period of time according to the requirements of the individual case and in general until a negative Wassermann reaction is obtained, if this is possible.

Forty of the seventy-four cases have been treated in this way and observed for a period of from three months to two years. As the cases differ so much in the types of lesions and length of treatment, they cannot be summarized to any advantage and the results of treatment are best seen by abstracting a few typical cases illustrating different points. We have given over two hundred intravenous injections of neosalvarsan and have never observed any bad or unpleasant effects besides those mentioned above.

EFFECT OF TREATMENT ON ACUTE LESIONS

There can be no question as to the value of neosalvarsan in acute syphilitic lesions with the exception of interstitial keratitis. In the acute joint lesions, ulcerations, general convulsions, torticollis, etc., the effects seem immediately to follow the first intravenous injection.

L. B., No. 3725, a girl of 17 months, was admitted for backward development. She had been normal until two months previously when she had an attack of convulsions. At the time of admission she was unable to stand alone and was apparently blind, not even noticing the milk bottle or a light. Attacks of general convulsions were frequent. Wassermann reactions on the blood and spinal fluid were positive. Neosalvarsan was given 1-14-13, 0.5; 1-17-13, 0.3; 1-22-13, 0.2 intramuscularly. The child was much better by this time and was beginning to notice objects. No attacks of convulsions since first injection. 1-31-13, 0.2, intravenously; 2-4-13, Wassermann positive; 2-12-13, 0.15, intravenously; 2-20-13, 0.2, intravenously.

Beginning about the first of February, 1913, there was rapid improvement and by the middle of the month the child was playing almost as a normal

infant. She was put on gray powder and on March 27 was discharged with a negative Wassermann. On April 24, one month later, there was a sudden return of symptoms and two days later she was readmitted. Between 12 o'clock noon and 9 p. m. there were ten attacks of general convulsions. She was then given 0.2 neosalvarsan intravenously which immediately stopped the convulsions. Inunctions of mercury were pushed for a month but no more neosalvarsan was used as the patient remained free from convulsive attacks. On May 17 the Wassermann reaction was negative and the patient was again discharged. In March, 1914 (fifteen months later), she was apparently normal although there have been "slight attacks of convulsions at times." She has taken gray powder intermittently.

R. C., No. 5043, a girl of 12 years, was admitted with a maniacal type of chorea about three weeks after the onset. She was unable to stand or walk and could not sit on a chair unless supported. Restraint was even necessary when she was in bed. Speech had been lost for several days. A family history of syphilis together with Hutchinson's teeth in the patient gave the idea of an underlying luetic infection. A dose of 0.4 gm. neosalvarsan was given a few hours after admission and a marked effect was noted within forty-eight hours. It was repeated two days later when a Wassermann reaction was strongly positive. Inside of a week the patient was up and about the ward and had lost most of the choreic symptoms. Neosalvarsan and mercury were continued for some time.

L. D., No. 4072, a 14-year-old girl, was admitted for acute pain and swelling of the right knee. One week later the ankle became swollen. A Wassermann taken two days previous to the involvement of the ankle was strongly positive. Neosalvarsan, 0.5, was given and in two days the swelling and pain had disappeared.

N. D., No. 3715, was admitted for an interstitial keratitis of five weeks' duration and an acute arthritis of the knee of two weeks. Wassermann, three plus positive. On Dec. 29, 1912, an injection of 0.9 neosalvarsan was followed by rapid improvement of the knee, but in a few days it became swollen and painful again. On Jan. 1, 1913, 0.9 neosalvarsan was given and followed by rapid relief. Treatment was continued with no return of the arthritis, but the interstitial keratitis showed but little improvement.

E. G., No. 6489, 8 years, admitted March 2, 1914, for acute arthritis of the right knee. Wassermann on March 5 was four plus positive. Neosalvarsan was given on March 7 and by March 11 all pain was gone from the knee and motion was good. She was given more neosalvarsan and discharged. Six weeks later the patient returned with an acutely swollen and painful left knee and the Wassermann was still four plus positive.

T. B., No. 3791, a boy of 6 years, was admitted with an extensive laryngeal ulcer of three weeks' duration. He was given five injections of neosalvarsan and within two weeks the ulcer had healed.

From these few reports the rapid action of neosalvarsan may be seen when the lesion is acute. The exception is apparently an acutely developing interstitial keratitis. In this condition it has an influence in some cases, but in our experience a long and extensive course of mercury is necessary in order to obtain much improvement.

TREATMENT AND CHRONIC LESIONS

We have been able to secure but little permanent effect from neosalvarsan nor have we observed any advantage from its use in chronic cases of the late type; that is, where a lesion such as a cerebrospinal syphilis or an interstitial keratitis has been present for

some time. As a matter of fact the most intensive treatment with combined neosalvarsan and mercury has been of little avail in these cases.

H. W., No. 3492, a boy of 14, was admitted for cerebrospinal syphilis (fixed unequal pupils, staggering gait, dementia, etc.), which was said to have first shown itself three years previously. Wasserman four plus positive. He was given 0.5 neosalvarsan in October, 1912, which was followed by inunctions of mercury. An injection of 0.9 neosalvarsan was given in December and the inunctions continued. In February, 1913, he was given two injections of neosalvarsan of 0.5 each and then gray powder was continued for several months. It was without effect on either the clinical condition or the Wassermann reaction. From time to time he has taken gray powder in large doses, but his condition to-day is worse than when treatment was started over twenty months ago.

In this same group must be placed the cases of hemiplegia following vascular changes and other conditions where structural changes have occurred. The only possible result of treatment in such cases is the prevention of further lesions.

TREATMENT AND THE WASSERMANN REACTION

It is not within the scope of this paper to enter into a theoretical discussion of the Wassermann reaction. For clinical purposes we look on the Wassermann reaction as a symptom of syphilis, comparable to an arthritis, a keratitis, a periostitis, etc. It is the most common symptom and present in such a large percentage of all clinically positive cases that we are inclined to be skeptical about the diagnosis of late syphilis in any untreated patient who has a negative Wassermann reaction. For example, we have had a case of interstitial keratitis in a boy who had marked Hutchinson's teeth. The Wassermann was repeatedly negative but because of the two classical symptoms of hereditary lues he was given a thorough antisiphilitic treatment which, however, was without effect. Later a rapid and marked improvement of the eye condition followed the use of tuberculin and in our opinion there is no reason for looking on this case as one of syphilis. A positive Wassermann reaction may be the only symptom of syphilis for many months or years (latent hereditary lues) and then other symptoms develop, as is shown both by the early history of some of our cases and the tests we have made on brothers and sisters of patients with manifest lues. It is quite difficult to get these patients with latent cases to take a course of treatment, but there is no reason why this symptom should be treated any less vigorously than a manifest lesion. Nothing definite is known of the future of these latent cases with a positive Wassermann and we are attempting to follow some which have not been treated.

The Wassermann reaction is stronger in hereditary lues than in any other form of syphilis and hence is correspondingly more difficult to make negative. Not only is this so but it is very apt to become positive again if treatment is stopped when it has been made negative as the result of treatment. We have not determined quantitative effects of the treatment on the Wassermann reaction.

N. D., No. 3715, a girl of 8 years, was admitted in December, 1912, for interstitial keratitis and acute arthritis. Wassermann four plus positive. The arthritis improved rapidly following two injections of neosalvarsan of 0.9 each followed by one of 0.5 and another 0.4. Gray powder, gr. 1 three times a day, was then given for three months when inunctions were started and continued for several weeks as the eyes did not improve. In May, 1913, the Wassermann was still four plus positive. Gray powder has been taken almost continuously since at the limit of tolerance and at times potassium iodid has been given. On Jan. 16, 1914, the Wassermann was still four plus positive and again on May 19, although the child has been given an intensive and uninterrupted anti-syphilitic treatment for eighteen months and the eyes have improved considerably.

C. M., No. 53166, aged 13 years, was first seen on July 16, 1913, for an interstitial keratitis which began one month previously. Wassermann four plus positive. He was given 0.5 neosalvarsan intravenously every other day for three doses and then put on gray powder. Three months later the Wassermann was still positive and the gray powder was continued. On March 6, 1914, the Wassermann was still four plus positive, although the eyes had improved very much with eight months' continuous treatment.

K. V., No. 4081, a boy of 7 years, with an acute keratitis, had a positive Wassermann on Sept. 23, 1912, at which time he could not distinguish fingers at 5 feet. He was given neosalvarsan 0.3 and inside of a week was able to make out pictures across a room. Two more doses of neosalvarsan were given, but as on March 14, 1913, the Wassermann was still strongly positive, three more injections of 0.4 each were given. A Wassermann taken five weeks later, or May 2, 1913, was still four plus positive. Gray powder—1 grain three times a day—was then given for three months but was without effect on the Wassermann. Eyes almost entirely well. This Wassermann, Aug. 1, 1913, was ten months after beginning treatment. The gray powder was then pushed to a point of salivation and kept up almost continuously until a *negative* Wassermann was obtained on Jan. 5, 1914, after fifteen months of vigorous treatment. Treatment was discontinued for two months and then a course of mercury given for one month. On May 19, 1914, six weeks after this was finished, the Wassermann reaction had again become *positive*.

At times it is not difficult to obtain a negative Wassermann reaction as in the following case.

G. G., No. 3443, an infant of 18 months, who was admitted for ulcers of the face and fingers (gummata) had a positive Wassermann Oct. 15, 1912. There was extremely rapid improvement following an injection of 0.22 neosalvarsan into the buttocks. This was repeated in fifteen days and the infant discharged one month later with a small nodule in the cheek the size of a pea. No other treatment was given. Five months later a Wassermann was taken which was strongly positive and the patient was given three intravenous injections of neosalvarsan of 0.25 each and discharged as there were no clinical lesions. Eight months later—fourteen months after first admission—the Wassermann was negative and in April of this year there had been no return of symptoms. This was one of the few cases with a permanent result following neosalvarsan alone and is decidedly exceptional in our experience.

In a treated case or a case under treatment in which the Wassermann has become negative, other symptoms of syphilis may develop, showing that the disease cannot be regarded as cured or quiescent from a negative Wassermann reaction alone.

E. P., No. 3995, a boy of 4½ years, was admitted for paronychia and malnutrition. No history obtainable, but the Wassermann was three plus positive on March 7, 1913. He was given seven intravenous injections of neosalvarsan (2 gm. in all) between this date and April 23, 1913. Inunctions of mercury were given to the point of salivation. There was marked improvement following the first few injections of neosalvarsan. In June and again in September he was given a course of mercury and on Oct. 24, 1913, (seven and one-half months after the first Wassermann) the Wassermann reaction was negative. In March of the present year he developed an alopecia which has become quite extensive. A Wassermann reaction on April 11, however, was negative, and again a few weeks later after a provocative dose of neosalvarsan.

SUMMARY

We have found the incidence of manifest hereditary lues of the "late" type much greater in proportion to the incidence of "early" syphilis than previous figures would indicate. The largest group of our cases (43 per cent.) exhibited lesions of the central nervous system, but we particularly wish to call attention to a group of cases with lesions associated as "rheumatic"—chorea, acute arthritis, torticollis, myalgia. By Wassermann reactions and the "therapeutic test" we have found that such lesions are not infrequently due to an hereditary syphilitic infection.

It has been our experience that acutely developing lesions respond promptly to intravenous injections of neosalvarsan, but that in order to obtain any permanent results and prevent the recurrence of symptoms an intensive and long continued mercurial treatment must be given in addition. The syphilitic infection—as measured by the Wassermann reaction—is most persistent, and although an intensive and uninterrupted antisyphilitic treatment has been given for nearly two years we have not been able to obtain a negative Wassermann reaction in some of our cases. Moreover, the Wassermann reaction has usually returned when treatment has been interrupted in those cases in which it has become negative as the result of treatment. We do not feel that it has been demonstrated as yet that an hereditary syphilitic infection of the "late" type can be eradicated.

St. Louis Children's Hospital.

ONE HUNDRED AND FORTY-ONE CASES OF RECURRENT VOMITING IN PRIVATE PRACTICE *

CHARLES GILMORE KERLEY, M.D.

NEW YORK

The cases reported have been seen in private practice during the past eight years. Cases seen in consultation with other physicians have not been included.

The history diagnosis was based on definite periodic attacks of vomiting, for which condition the patient was brought to me.

Recurrent vomiting, in a vast majority of the cases, we found occurs in the offspring of those who for two or more generations have not been occupied with manual work. The recurrent vomiting patients are the offspring of those who have had business or professional occupation.

SUMMARY OF THE FEATURES OF CASES SEEN

Average time cases were followed was 104 weeks.

Sex: Seventy were boys; seventy-one were girls.

Family History: Rheumatism in one or both parents in forty; sick headache and bilious attacks in forty.

Appetite: In 31 per cent. was normal; in 69 per cent. it was indifferent; in 59.5 per cent. there was constipation.

Previous Feeding in 120 Cases: Twenty-one patients were nursed by mother nine months; forty were nursed by mother six months; four cases had been wet-nursed; sixty-nine had been difficult feeders on cow's milk and had been given the usual trial of foods.

Recurrent colds had been present in 41 per cent. This information was usually volunteered. In twelve there was definite history of eczema; six had habit tic. In fourteen there had been or was enuresis. In thirteen there had been rheumatism.

Urine: Nothing was known as to the condition of the urine in the attacks before coming under observation. The presence of acetone in the later attacks was noted with very few exceptions, but there were exceptions. A child in an attack may show acetone and in the next attack the urine may be free.

Onset of the Vomiting Seizures: Thirty-seven occurred during the first year; twenty-four occurred during the second year; twenty-one occurred during the third year. Onset in the youngest was 6 months. In three the onset was during the eighth year.

Duration of Interval Between Attacks in 119 Cases: Under 2 weeks, 22; from 2 to 4 weeks, 27; from 4 to 6 weeks, 10; from 6 to 12 weeks, 42; from 3 to 6 months, 40.

Duration and Severity of Seizures: The severity of the attacks varied widely; in some the child would vomit but two or three times. These usually represented the short-interval cases. In others the vomiting was protracted and severe. The average was three and one-half days. The longest seizure under observation continued thirteen days.

* Read at the annual meeting of the American Pediatric Society, Stockbridge, Mass., May 28, 1914.

The average interval in 118 cases was eight and one-fourth weeks.

Temperature: 102 F. or over in 30; 103 F. or over in 10; 104 F. or over in 6; 105 F. or over in 3. In the remainder there was an elevation of from 100 to 102 F.

In taking the history in fifteen cases, the mother or attendants volunteered the information that the child had a peculiar breath at the time of the attack which we interpreted as the so-called "acetone breath."

Onset: Average age in 121 cases was 2 years and 8 months; average number of attacks in 99 cases had been 9; average age brought for treatment was 5 years.

Results: Of cases in which there were no attacks after beginning treatment: Forty-one were followed for from two to eight years. Of these forty-one, twenty-six were followed from three to eight years and fifteen were followed from two to three years. Fifteen were followed from one to two years; nine cases were followed from six months to one year; eighteen cases were followed less than six months. Several of the latter are recent cases in which decided gain in weight and general improvement has occurred. In nine cases there was very much improvement; the attacks were mild and comparatively infrequent. Of these eight were followed for from two and one-half to eight years; one was followed eighteen months. In thirty-three cases there was improvement; the attacks less frequent and less severe. Of these thirteen were followed from two and one-half to eight years; six were followed from one year to eighteen months. The remaining fourteen of this group were followed for varying periods under one year, but the records show that a decided impression had been made on the seizures.

In sixteen cases there was no apparent improvement. In some the treatment was indifferently carried out and the patient was dismissed. In others, no apparent impression was made on the disease and the seizures continued as before.

I have an unimproved case that has been under treatment for three years without benefit. The attacks continue to be very severe at from ten to twelve weeks' interval. I only recently was successful in having massage and exercise treatment instituted.

Another boy now aged 6 has attacks of either periodic fever, bronchitis or recurrent vomiting, rarely going for three months without an explosion of some kind. He has been my patient since he was 6 months of age.

In a vast majority of the cases the recurrence will be completely controlled if continued family cooperation is secured. A diet and living regimen will be followed faithfully by some parents as long as they can be kept anxious about the patient. When the child has passed three or four vomiting periods, the use of forbidden articles of food is often gradually resumed; the former methods of living are more attractive than the regimen laid down.

The association of recurrent vomiting with other forms of illness is interesting. As mentioned before, 41 per cent. of these children were subject to repeated bronchitis, usually of the spasmodic type, and not infrequently the bronchitis and the vomiting occurred simultaneously. Acetone was not present in these cases unless gastric symptoms were present. In others, the attacks will be distinct and separate. In one

patient there was in nearly every attack an acute spasmodic laryngitis; bronchial asthma very urgent followed and this again was followed sometimes, but not invariably by repeated vomiting. This child had suffered severely with eczema when an infant. Two boys, brothers, were of particular interest in that they had the attacks simultaneously, beginning with tonsillitis, followed by bronchitis and asthma and ending with recurrent vomiting lasting for a day or two. In a few cases the recurrent vomiting attacks were replaced by high fever for three or four days, with acetoneuria and without other symptoms.

Two girls, aged 5 years, both in wretched condition, had mild vomiting every week or ten days. In both the acetone breath and acetone urine were continuously present.

The only fatal case seen by me and not included in the above statistics was in a girl 7 years of age living in a New York suburb. There had been previous attacks at about from three to six months' intervals. This attack was particularly severe, no fever but frequent and violent emesis. The vomiting had continued about four days when I saw her. At this time there was considerable exhaustion, but the child was fairly bright, answered questions and talked freely. I endorsed the attending physician's treatment, made a favorable prognosis, and the child died in five hours. Apparently, death was due to respiratory paralysis.

Three patients had been operated on for appendicitis in Paris without relief. A normal appendix was removed in each case. In three it was necessary to resort to morphin hypodermatically to control the vomiting seizures.

MANAGEMENT DURING THE INTERVAL

The management in the main was the same in all, and one reason for reporting only the cases seen during the past eight years is that during this period practically the same interval management has been carried out.

Diet: If the case is a pronounced one, the patient is given a diet with few restrictions, except that cow's milk, butter, cream and sugar are omitted. One egg is allowed perhaps every third day. Saccharin is permitted as a sweetening agent in some and very little sugar in any case.

Three meals daily are allowed with nothing between meals. Red meat is given scantily three times a week. Poultry and fish are given at other times. In some skimmed milk is allowed scantily, never more than one pint daily, often less. Puddings are made with skimmed milk. A grave error in our management of many children is the free use of cow's milk, butter, ice-cream and sugar. I could present dozens of records showing surprising gain in weight and marked improve-

ment in the general well-being of the patient after a considerable withdrawal of milk, cream and sugar from the diet.

The period of lactation in the human being is at the most a year and then the child is ready for other food than milk. I believe that the average well child would thrive far better if he were to get not more than one pint of milk daily after the fifteenth month. Sugar was not used except as a condiment as we now use honey, until three hundred years ago. Unknown millions lived their span without it.

Medication: The further treatment consists in the internal use of salicylate of soda, bicarbonate of soda, independent or in combination as advocated by Rachford. In a pronounced case I give 5 grains of sodium salicylate with 10 grains of sodium bicarbonate three times daily at five-day intervals, or 20 to 30 grains of the sodium bicarbonate daily for a month or two at first. This drug treatment is carried on with rest periods for months and years as the case may require.

Bodily Exercise: A very important factor in the management is in arranging daily physical exercise, such as riding horseback or the bicycle and walking so many street blocks a day. A warm bath and a brisk rub are given at night, and last but not the least important feature in the treatment is the use of physical therapeutics. In severe cases I use if possible daily massage together with various body manipulations and exercises, the latter sufficient to make the child perspire, but not to the point of exhaustion. The advantage of this phase of the treatment was called to my attention by Dr. W. P. Northrup.

Bowel Function: A daily evacuation of the bowels is insured by suitable measures.

Some children I take out of school. For others I advise a modified rest-cure, which means in bed until 10 a. m., rest one and one-half hours after dinner and in bed and lights out at 6 or 7 p. m. The nervous element in these cases is not to be forgotten. If the attendant is not agreeable to the patient her services are dispensed with. In some a temporary elimination of the mother has been of assistance. The precipitation of an attack by fatigue and fright is not unusual.

The regulation of the life and habits aids materially in the management, but is of little or no use if the carbon content in the food is not reduced to the oxidizing possibilities.

MANAGEMENT DURING THE ACUTE VOMITING ATTACK

I find that in the vast majority of the cases, a weak solution of sodium bicarbonate is best retained in the strength of 5 grains of the bicarbonate to 8 ounces hot water. This is given freely.

As laxatives the magnesia preparations are best retained and are used when a laxative is required. Calomel or mercury with chalk will

often increase the vomiting. In other cases their use supplies very material assistance. When the vomiting has continued for twenty-four to thirty-six hours the patient is given colonic flushings with sodium bicarbonate, 2 drams to 8 ounces of water at eight-hour intervals. The solution is best retained if it is given warm (105 F.), the tube inserted from 8 to 12 inches.

Feeding: Nothing is gained by attempts at forcing the feeding. When the child is ready for food, he is given barley or rice gruel with dried bread crusts or unsweetened zweiback.

Judging from the results obtained through the withdrawal of highly energized foods and in the use of active and passive exercises it would seem that the chief error in most cases rests in a defective oxidation, or in the giving of food substances of high carbon content in excess beyond the powers of normal oxidation.

In this connection the views of Francis Hare¹ are particularly interesting. Hare states that carbon intake must be offset by carbon expenditure or energy intake with compensating energy expenditure, if "hyperpyremia" (excess of fuel in the blood) is not to occur. When physiologic functions are deficient in maintaining a balance, and an excess of carbon or hydrocarbon is not wholly applied in the manufacture of additional fat, bile, milk or other secretion, or lost by exercise or menstruation, a pathologic function is then necessary to free the system of its excess of fuel. As such so-called pathologic functions, Hare mentions gout, migraine, gastralgia, bilious attacks, epilepsy and asthma, all of which operate through either a reduction of income or an increase of expenditure by vomiting, muscular action or fever, periodic in character. These attacks of migraine have been observed alternating in the same individual with attacks of gout; gout has subsided with the development of glycosuria, and women (according to Garrod) show greatest liability to the development of gout shortly after the menopause, one decarbonizing process replacing another.

I am not convinced of the reliability of this theory in its entirety, but find it peculiarly in harmony with the clinical facts under presentation, and (while not forgetting for a moment that proteid anaphylaxis (Meltzer) and reflex neuroses from various abnormalities are still to be considered as operative causes in such affections as asthma, recurrent vomiting and migraine) I wish to emphasize the following suggestive points:

Eczema, spasmodic laryngitis, cyclic vomiting and recurrent bronchitis and asthma are all notoriously frequent in children of gouty or rheumatic ancestry.

1. Hare, Francis: Carbon Factor in Gout, Med. Rec., June 17, 1905.

All these conditions are met less frequently and with diminishing severity at the age of puberty when the processes of combustion and tissue building are at their maximum.

While two or more of these so-called pathologic functions are not ordinarily observed simultaneously in the same child, not a few children suffer from a number of these conditions in alternation over a period of years. In other words, the processes seem to be mutually compensatory.

In the winter months, when activity is lessened and perspiration is least, every one of the conditions mentioned is intensified.

Finally, in every instance, diet (as the cases show) is a most prominent factor influencing the susceptibility of the patient.

The statistics as presented were prepared from my case histories by my associate, Dr. Frank Elmer Johnson, to whom I wish to express my indebtedness.

132 West Eighty-First Street.

MYATONIA CONGENITA OF OPPENHEIM*

AUGUST STRAUCH, M.D.*

CHICAGO

Since Oppenheim¹ has described and outlined the clinical picture of this disease, a number of subsequent observations by this author and others have broadened the clinical aspect, adding new features to those first described.

Some observations were made, in which not only the muscles of the extremities were involved but also those of the neck and back; and in a series of cases the flaccid pseudoparalysis involved not only the musculature of neck in addition to the more commonly affected extremities, but also that of the whole trunk simultaneously, so that with the exception of the diaphragm all muscles supplied by the spinal nerves appeared paralytic.

The assertion that the muscles supplied by the cranial nerves remain intact in this disease had to be modified as the result of additional observations. A certain degree of participation of the cranial nerves especially of the facialis is in a few histories at least cursorily indicated. Pollak² published a report of a well-observed case with involvement of the musculature of the facial and hypoglossus nerves in addition to the affection of all the spinal nerve muscles with the exception of the diaphragm. Cases of facial affection are described by Tobler,³ Collier and Wilson.⁴

REPORT OF CASE

The following case seen by me this year deserves here a more detailed description, not only because it adds to the small series last mentioned, but also for reasons later to be dwelt on:

History.—Second child, girl, born in America, April 5, 1914, of healthy Russian Jew parents. Their first baby died when 3 weeks old, presumably from cephalematoma, which possibly became infected, as baby was paralyzed before death. Family history negative; no intermarriage. Spontaneous normal birth at full term. Mother had felt quickening during this pregnancy as in the first. The new-born, according to a woman friend, cried loudly immediately after birth, and was able to move during the first week of life;

*From the Central Free Dispensary, Rush Medical College, Chicago.

1. Oppenheim: *Monatschr. f. Psychiat. u. Neurol.*, September, 1900, viii; *Berl. klin. Wchnschr.*, 1904, No. 10, p. 255; *Lehrbuch der Nervenkrankheiten*, Edition 5, Part 1, p. 242.

2. Pollak: *Arch. f. Kinderh.*, 1910, liii, 373.

3. Tobler, L.: *Ueber kongenitale Muskelatonie (Myatonia congenita Oppenheim)*, *Jahrb. f. Kinderh.*, 1907, lvi, 33.

4. Collier and Wilson: *Amyotonia Congenita*, *Brain*, 1908, xxxi, 1.

the mother herself can make no statement on this point. She remembers at least, however, that in the second week of its life the baby moved only a little and very slowly and was completely paralyzed from the third week. The baby's cry was only a low, feeble one, the facial muscles showing no contractibility, "it cried only with its voice, but without its face." Abdominal respirations were labored. She was always a quiet baby. Stools were irregular, constipated, appetite and sleep good; breast-fed. These conditions did not change noticeably with the exception that the baby has exhibited during the last five or eight days a smile, and a slow, feeble mimical action of the face when crying.

Examination.—July 4, 1914: Girl, well nourished, face of healthy color. Panniculus adiposus well developed, skin warm, of healthy rosy tint. The baby lies on its back with all extremities immovable; when lifted up, they drop as lifeless to the pillow. The legs are rotated outwardly. Only very minimal slow, feeble movements of the fingers, toes and ankle-joints, spontaneously or on needle-pricks, to which the baby responds with very feeble crying. The abdomen is very prominent, tympanitic, the wall very flabby and soft. Respirations very frequent, from 70 to 80 per minute, irregular, abdominal, the diaphragm acting vigorously with marked inspiratory protrusions of the upper part of the abdomen and with retractions of the lower part of the thorax. The hand laid on the abdomen meets a marked resistance from the protrusion during inspiration. If the child is lifted up underneath the shoulders, the latter are pushed up to the ears on account of the flabbiness of the tissues; the arms and legs swing in complete flaccidity, the right arm thereby rotates into somewhat extreme position, as if without sufficient hold in its shoulder-joint. In the other joints of the extremities there is to be noted no hypermobility. If the body is brought into sitting position, the head on account of weakness of the neck musculature wabbles and drops helplessly to any side into extreme positions as in a cadaver, the trunk falls forward, forming a marked kyphosis. The limbs are full and round. The tissues of the upper extremities are markedly flaccid, so that the muscles are not discernible from the panniculus adiposus; those of the lower extremities that are well developed, have an almost normal turgor; their panniculus adiposus is solid and the underlying musculature can be palpated only very indistinctly. There is nowhere any atrophy to be noted. Though the face shows good muscular contractions during crying, yet these occur with appreciable slowness, and in the quieter intervals the infrequency and feebleness of the mimic display gives to the face a certain immobility and blank expression. Smiling occurs only very rarely and very feebly. Both eyes follow a flame or bright object; in lateral positions the bulbs show horizontal nystagmus, when fixating. Pupils react promptly to light. The baby recognizes its mother. My finger introduced into the baby's mouth causes a vigorous contraction of the lips and pressure by the sucking tongue. Stools constipated, appetite normal.

Reflexes.—Patellar reflex, Achilles-tendon reflex, Babinski, reflexes of the abdominal wall and soles of the feet are entirely absent, biceps-tendon reflex doubtful. No fibrillary contractions. No mechanical irritability of the muscles of the extremities on tapping with the percussion hammer.

Electric irritability: The neuromuscular irritability, examined on the extremities and trunk with strong faradic current is entirely absent; also no response to single shocks. (Galvanic test see July 25.)

A gross lesion of the sensibility can be excluded; but one's impression is that crying is less on faradic irritation of the lower extremities than of the upper, and that the patient bears strong faradic stimuli easily.

Treatment.—Daily faradic treatment, massage and sea-salt bath.

Course of Disease.—July 21: Baby moves the left arm occasionally, being able slowly to bring the hand spontaneously even to the mouth, and hold a morsel of bread. Very rarely the right arm is moved, slowly and only slightly in the elbow. The toes and fingers seem to show a slight improvement of mobility, if there is any change at all.

July 25: Mother makes the statement that the baby can be induced to smile more easily. The crying is somewhat louder, and when quiet there is a beginning of a certain mimic display. Electric reaction: The examination of the muscles of the abdomen and the extremities reveals a complete lack of (neuromuscular) reaction on strong faradic current. The small muscles of the dorsum pedis contract moderately on strong galvanic current stimulation; quadriceps cruris and the muscles supplied by the peroneus nerve contract feebly. The contractions, however, are quick and short, not as in degeneration. The cathode closure contraction is somewhat stronger than the anode closure contraction.

July 29: During longer observation baby shows infrequency or almost entire absence of mimic display, but when pricked painfully shows good contractions of the facial muscles in crying. Horizontal nystagmus present especially in lateral positions of the eyeballs in fixating. The baby's legs are still motionless under ordinary conditions, but on several occasions they have been brought actively side to side in the bath, when previously they had been crossed over the shin-bone by the mother or passively bent in the knee-joint.

August 5: Baby is able to flex and somewhat extend the knee and hip-joints when in the bath, not otherwise. There is a decided improvement of both arms; occasional movements also are possible in both shoulder-joints, though less in the right one. Nystagmus. Crying with feeble voice. Respiration abdominal.

August 11: Condition the same: Crying very feeble. Spontaneous mimic display rare. Slight edema of dorsum pedis on both sides. The tissues of the legs are softer than before.

September 4: A moderate degree of flabbiness of the tissues of the legs has become evident; otherwise the condition is the same.

Summarizing the principal clinical features, we have flaccid pseudo-paralysis of the muscles of the extremities and the trunk with the exception of the diaphragm, and an involvement of the facial muscles, with a tendency toward improvement. There is absence of the faradic and diminution of the galvanic irritability of nerves and muscles, but no atrophy. Skin-reflexes and tendon-reflexes are absent.

By this symptom-complex this case can easily be identified with the clinical picture of Oppenheim's myatonia congenita whose features may be reproduced here, before I dwell on a few factors of my case that are worthy of special consideration.

SYMPTOMATOLOGY

The disease occurs in the earliest infancy without known causes. That the beginning may occur during the intra-uterine life is indicated by the frequent statement of the mothers that during pregnancy they had felt no movements of the child. The symptoms exist from birth and in most cases are noted during the first days of life. With attention lacking or inefficient, the conditions may escape the notice of the family for weeks or even months until the failure of the baby to learn to stand or walk reveals the motor disturbance, as is also often the case in congenital cerebral paralysis (paraplegia) or early poliomyelitis anterior. In a few cases, in which even under good observation the symptoms were not manifest at birth, various diseases as bronchitis,

pneumonia (Leclerc⁵) or diarrhea (Comby⁶) soon caused their appearance. In such cases we may consider these intercurrent affections partly responsible through their general weakening result, only in making the manifestations of myatonia more conspicuous. Yet Rosenberg⁷ observed a case in which the weakness of the legs appeared as late as in the eleventh month; Collier and Wilson⁴ report a similar observation and conclude that the disease may develop at any time in an apparently normal child in the first year of life.

The most conspicuous feature is the inactivity of the child and the flaccidity of the musculature. The affected extremities, the arms often and the legs invariably and in a greater degree, lie on the pillow as if paralyzed, because of the extreme weakness of the musculature; they remain motionless in the most uncomfortable positions in which they are brought during the examination. Perhaps the distal parts, namely, the fingers and toes, retain a slight spontaneous residual mobility or on needle-pricks. The movements in the other joints, should they be present, are slow and weak in the more pronounced cases, the muscular contractions being without energy and real locomotor effect. The limbs, lifted by the examiner, drop on the support as if lifeless. The affected muscles are as a rule markedly flaccid, hypotonic or atonic, of soft consistency, but not atrophic, as in poliomyelitis anterior, or in neuritic paralysis; nor are fibrillary contractions to be observed.

It is impossible to distinguish by the touch between panniculus adiposus and muscles; the structures from the skin down to the bone seem to be one soft homogeneous substance. In a few cases, however, a certain degree of reduced volume of the muscles has been clinically noted, as by Batten, Collier and Wilson, Marburg and Schlivek; which fact does not surprise us, if we consider the inactivity of the muscles more or less absolute — apart from the nature of the disease. In other cases an abundant development of the panniculus adiposus renders it impossible to make a decision, and marked reduction of muscle with proliferation of connective and fat tissue has been revealed anatomically in cases in which the clinical appearances indicated well-developed muscles.

The joints may be loose, flaccid and more or less flail-like, so that the limbs are passively movable like loose appendages. Where the back and neck musculature is involved, the body, if brought to a sitting position, will fall forward and double up "as if made of rubber" with the formation of an extreme kyphotic curvature of the spinal column, and the head will wobble and fall to any side. Standing is impossible,

5. Leclerc: *Gaz. d. hôp.*, 1907, No. 141.

6. Comby: *Bullet. Soc. pédiatr. de Paris*, October, 1907, p. 149.

7. Rosenberg: *Ueber Myatonia congenita*, *Deutsch. Ztschr. f. Nervenh.*, 1906, xxxi, 130.

as the lower extremities collapse helplessly. Where the respiratory (intercostal) muscles participate, the respiration has lost its costo-abdominal character and becomes purely abdominal, the diaphragm acting vigorously in compensation. The weakness of the abdominal wall musculature manifests itself in more or less marked softness, protrusion and flabbiness of the abdomen and may cause constipation.

The reflexes are as a rule absent or diminished; likewise the neuromuscular irritability to both currents, but degeneration reaction will not be found. The sphincters of anus and bladder and the vasomotors are normal, the sensibility rarely (cases of Rothmann,⁸ Collier and Wilson⁴) is slightly affected. The affection in its typical form is the antipode of Little's disease.

The course of the disease is chronic with a tendency toward improvement, a part of the more severe manifestations being capable of a gradual reparation during months or years, though perhaps in no case as yet has a complete recovery been observed. The improvement is mostly slow, to be of any amount, takes years, but even after a standstill for years, improvement can take place. The upper extremities apparently always recover first, and may gain even a normal function. The disease is not dangerous of itself, but it exposes the individual — as *dystrophia musculorum progressiva* — in a high degree to pulmonary affections, and their prognosis is markedly impaired through the weakness of the respiratory muscles. In fact, that pneumonia and bronchitis are among the chief causes of the high death-rate among these individuals is no mere accident. It is worthy of note that this clinical picture has not been observed in the adult, a fact partly explainable by the great dangers of accidental intercurrent diseases.

The more limited the atonia is, either from the beginning or as the result of improvement, the more limited and altered will be this picture of infirmity. Further attention should be given to the existence of rudimentary, abortive forms of the disease. From the literature we note the fact that considerable differences in the intensity of the symptoms undoubtedly exist. In some cases with hypotonia there were indeed only minor degrees of paresis. It is probable that some hypotonic conditions in infants may have a cause identical to that of the fully developed, pronounced pictures of *myatonia congenita*, especially if muscular weakness is manifested in the lack of energy of some movements.

NATURE AND PATHOLOGY

Oppenheim referred the *myatonia* to a retardation of development of the musculature, without excluding the possibility of a developmental retardation of certain nerve centers, especially of the ganglia

8. Rothmann: *Monatschr. f. Psychiat. u. Neurol.*, 1909, xxv, *Ergänzungsheft*, p. 161.

of the anterior horns and their function. The possibility of a gradual development toward normal or almost normal function, but also of an aggravation — though very rare — is admitted.

The anatomic findings have been various; they place the affection near the group of the primary myopathias — dystrophia musculorum progressiva — which latter have a close relationship to the spinal myopathias; but clinical reasons so far do not allow us to classify myatonia with dystrophia progressiva. The most frequent alterations concern the musculature. The pathologic-anatomic findings of Spiller are in support of Oppenheim's view; the affected muscles were little developed amid an hyperplastic interfibrillary fat tissue; the muscle-fibers were very narrow, their longitudinal striation indistinct; the nervous system was intact.

Rothmann⁸ observed a marked proliferation of the interstitial connective and fat tissues; the muscle-fibers were partly atrophic. Also Reyher and Helmholz found the muscles, especially of the legs, deeply affected; the fibers were partly thin, partly hypertrophic, their transverse striation partly indistinct, partly lacking.

In the cases of Baudouin⁹ and Collier and Holmes,¹⁰ the muscular changes resembled much those in primary myopathias. They observed also congenital hypoplasia of the cells of the anterior horns. In some of these cases the cells were markedly small and underdeveloped; or their number was decreased, but without any sign of inflammation; the peripheral nerves had defectively developed medullary sheaths, a condition which was considered a sign of underdevelopment.

In Rothmann's case there was extensive atrophie (*Schwund*) of the motor ganglia throughout the medulla spinalis. Also the white substance was not intact. The cross-section of the medulla spinalis was small *in toto*. The transverse section of the peripheral nerves was very narrow; there were also pathologic changes in the nuclei of a few cranial nerves (hypoglossus, vagus); these, however, had given no clinical symptom.

Thus really the affection may concern the whole peripheral neuron, the aplasia or hypoplasia involving in the one case this, in another case that segment of the neuron, including the muscle.

Bing,¹¹ differing from Spiller,¹² found a normal structure of an excised particle of muscle with the exception of perhaps a somewhat increased number of nuclei, and conceives the nature of the disease

9. Baudouin: La myatonie congénitale (maladie d'Oppenheim), *Semaine méd.*, 1907, xxxvii, 241.

10. Collier and Holmes: *Brain*, 1909, xxxii, 269.

11. Bing: Ueber atonische Zustände der kindlichen Muskulatur; vorläufige Mitteilung, *Med. Klin.*, 1907, iii, 10.

12. Spiller: *Myatonia congenita*, *Penn. Med. Bull.*, 1905, xvi, 342.

to be an inhibition of the development of the spinocerebellar nerve-tracts that regulate the tonus.

Vierordt thinks of a diminution of functional responsiveness for central and peripheral stimuli of the cells of the gray anterior horns of the medulla. The clonic spasms in the cases of Sorgente¹³ would be explained by stimuli of maximum intensity.

Kaumheimer¹⁴ draws the conclusion, from the histologic examination of a case, that myatonia is an entity which must be considered either as a toxic or endogenic affection, while the doctrine of inhibition of development or of inflammatory processes being the pathologic basis of myatonia must be discarded. The process has not necessarily found its completion at birth, but may cause alterations of the muscles even months later.

TREATMENT

The tendency of the disease toward partial or more pronounced spontaneous improvement renders it difficult to decide the contributing effect of any treatment; in addition to this, the descriptions of most cases in the literature represent merely snapshot pictures, so to speak. But it often seems as if a more pronounced improvement had taken place during treatment with electricity and massage, extended persistently over a long period.

COMMENT ON AUTHOR'S CASE

My own case is of great interest because of the involvement of the facial muscles, manifesting itself in lack or weakness of the mimic display; this was replaced by a certain degree of immobility, which improved before the other symptoms. The crying was markedly feeble, which fact finds its explanation in the involvement of the respiratory muscles, especially of the expiration musculature, a symptom also observed by Pollak,² Berti,¹⁵ Baudouin,⁹ Lugenbühl.¹⁶ The high frequency of the respiration and the vigorous inspiratory protrusion of the abdomen point also to a weakness of the intercostal muscles, that show retractions during inspiration.

It is noteworthy that, though the pseudoparalysis was more marked and more persistent in the lower extremities, their turgor or tonus was almost normal for the first four months, while the entire upper extremities with their more visible improvement manifested a pro-

13. Sorgente: Due casi di atonia muscolare di Oppenheim, *Pediatrics*, 1906, xiv, 358.

14. Kraumheimer: *Jahrb. f. Kinderh.*, 1913, lxxviii, *Ergänzungshft.*, p. 170.

15. Berti: Contribuzione alla atonia muscolare congenita di Oppenheim. 3. adunanza della sezione Emiliana della Società Italiana di pediatria, Dec. 4, 1904; *Pediatrics*, 1905, p. 134.

16. Lugenbühl: *Deutsch. med. Wchschr.*, 1907, p. 1439.

nounced atonia; the flaccidity of the shoulder-blade musculature permitted passive motions upward or medianward to the ears. While Cassirer¹⁷ claims that in most cases the proximal muscles of the extremities are less affected than the distal ones, a number of cases have presented the reverse conditions (Kaumheimer,¹⁴ Kundt,¹⁸ Rosenberg⁷). To the latter group belongs also my case; only the fingers and toes were slightly movable at the first observation. The explanation of this may be that for the movements of small parts, such as the distal ends of the extremities, less strength is required. Similarly I could observe the first signs of improvement in the mobility of the legs while the baby was submerged in the bath, which diminished sufficiently the motion-inhibiting effect of friction and gravity for the at first only minimal functional capacity of the legs. The very obvious flabbiness of the abdominal wall and the softness of the tympanitic abdomen indicated an involvement of this musculature; there was also constipation. The neck and back musculature being involved, the pseudoparalysis concerned all the spinal nerve muscles with the exception of the diaphragm.

Nystagmus, as in my case, was noted also by Koch¹⁹ and was referred by him to a congenital defect of eyesight. Whether this ocular symptom in my case should be considered as a manifestation of a congenital weakness of the external muscles of the bulbus, similar to that observed in lesser degrees of paresis of an extra-ocular muscle, or of a functional exhaustion, similar to the nystagmus in miners, or whether it should be regarded of central origin, cannot be decided with certainty. I am inclined to consider in my case the presence of weakness of extra-ocular muscles as a condition analogous with those of other muscles, affected in myatonia. A defect of eyesight in my case may be excluded by the fact that the child fixates well and recognizes persons, responding after improvement to the smile of the mother.

An interesting feature resulted from the electric examination of the nerves and muscles; though the irritability even to strong faradic currents was completely lost, there was nevertheless present a somewhat lessened irritability to the galvanic current; differing from degeneration reaction, however, the contractions were quick, short, though weak, and the cathode closure contractions were somewhat stronger than the anode closure contractions. As usually reported, the irritability of the muscles and nerves to the galvanic as well as the faradic currents in myatonia congenita of Oppenheim is found either absent or much decreased; in the case of Bing¹¹ the reaction was almost normal; in

17. Cassirer: *Lewandowsky's Handbuch der Neurologie*, 1911, ii, 230.

18. Kundt: *Ueber Myatonia congenita*, Inaug. Diss., Leipsic, 1905.

19. Koch: *Jahrb. f. Kinderh.*, 1913, lxxviii, *Ergänzungsheft*, p. 305.

that of Muggia²⁰ there was normal neuromuscular irritability. No qualitative alterations of the contraction formula is to be observed; Cassirer, Oppenheim, Rosenberg and others never found degeneration reaction; Rothmann, however, saw a rather sluggish contraction in his case.

Collier and Wilson described a special form of alteration of the electric reaction, which they declared was characteristic of myatonia, and they termed it "amyotonic reaction," and Chène concurs in this view. According to the observations of these authors the muscles react to the faradic current with diminished irritability, while to the galvanic current not only are the formula and character of the contractions normal, but also the quantitative alteration is only moderate. This special reaction is declared to be demonstrable to a certain degree in every muscle, most markedly, however, in the muscles most affected by the pseudoparalysis. The reverse of this modus of electric reaction was encountered by Koch, viz., the decrease of irritability was more marked for the galvanic than for the faradic current.

There exists no differential diagnostic difficulty in our case. Poliomyelitis must be excluded by the congenital character, the absence of febrile beginning, of vasomotor anomalies, the absence of degenerative atrophy and degeneration reaction, and by the symmetry and extent of the motor disturbances. The muscles in poliomyelitis recover rather by groups and the stage of reparation is much shorter. Pseudoparalysis rachitica is out of the question.

The extreme rarity of acute generalized polyneuritis at this age militates against this disease, also the absence of an etiologic factor (diphtheria), of pain or sensible disturbances of a higher degree; the absence of disturbances of the heart-action and deglutition, and the lack of degenerative atrophy.

In dystrophia musculorum progressiva we would expect a later onset, possibly a hereditary factor, gradual progress, the presence of localized myatrophia, perhaps hypertrophic and pseudohypertrophic muscles and no participation of the distal muscles, especially of hand and foot, which is rare in dystrophia. In Werdnig-Hoffmann's spinal atrophy of muscles we would have steady progress, an exact localization of atrophic paresis (proximal distribution) and degenerative reaction.

4557 Broadway.

20. Muggia: Adunanza della sezione Piemontese della Società Pediatrica Italiana del febbraio, 1903; *Pediatrics*, 1903, p. 179.

REFRACTORY OR SO-CALLED "FAST" CASES OF MENINGOCOCCUS MENINGITIS *

HENRY HEIMAN, M.D.

NEW YORK

It is well known that since the introduction of the antimeningitis serum by Flexner in 1906, the mortality of meningococcus meningitis has decreased from 75 or 80 per cent. to 25 per cent. or less. Despite this fact, it is obvious that in a small percentage of cases the treatment of this disease has not yet reached perfection. That this small number of cases does not respond to the serum, in spite of its accurate and prolonged use, gives us food for thought and compels us to inquire into the causes of the occasional failure with this method of treatment.

CAUSES OF OCCASIONAL FAILURE

These causes may be grouped as follows:

1. *Fulminating Cases.*—The endotoxins of the meningococcus may be so virulent as to make neutralization by the antimeningitis serum impossible. The action of the serum is dependent on the presence of a number of immune substances, bacteriolysins or antibacterial substances, bacteriotropins (opsonins) and antiendotoxins. When those substances are not present in sufficient quantity or are not of sufficient potency to overcome the endotoxins of the invading organism, we have the fulminating cases which practically always end in death, despite early diagnosis and prompt treatment. It is questionable whether a serum of sufficient concentration or strength can be obtained to combat successfully this rapidly fatal type.

2. *Incomplete, Insufficient or Unskilled Use of the Antimeningitis Serum.*—It is needless to dwell on this cause of the failure of the serum to cure, for it is a matter of common knowledge that, in general, the mortality statistics are the lowest when based on the experiences of the most competent observers and workers in this field.

3. *Unstable Nervous System.*—In infants, lack of success is often due to the existence of an unstable and delicate nervous system and to the early development of acute hydrocephalus.

4. *Intercurrent Diseases.*—Complications having no direct connection with the disease, as tuberculosis or pneumonia, may produce a fatal result, in spite of the beneficial action of the serum.

* Read before the Section on Diseases of Children at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

5. *Refractory Cases.*—Though few, these cases do occur and must be considered as constituting a distinct type. Although the meningococcus is found in the spinal fluid of these patients, the cases are little or not at all influenced by the injection of the serum. On that account they run a prolonged course of weeks or months, usually with high, septic temperature and occasional remissions in symptoms, until they finally result either in death or in a gradual protracted recovery. They are the "fast" cases, so called by Flexner, because they are supposed to be due to the existence of strains of meningococci which are fast to the serum employed.

It is only in recent years that fundamental biologic distinctions have been made between the various strains of the meningococcus. One strain is more resistant to solution by immune serum; another is more easily digested by the intraleukocytic enzyme; another more virulent when injected into animals—differences formerly never recognized. When this is taken into consideration, it is readily seen why certain cases do not respond favorably to the ordinary antimeningitis serum—they are produced by a strain of the organism which is refractory or fast to the serum used. They must not be confused with the type of cases described by Dopter, in which the clinical course is the same, but in which the infecting organism is not the meningococcus, but the closely allied parameningococcus, which possesses specific agglutinins and precipitins, does not react to the ordinary antimeningitis serum, but does respond beneficially to the serum prepared from its own cultures.

The following are reports of two refractory cases of meningococcus meningitis:

CASE 1.—M. S., aged 6. There had been no previous illness. Two days before admission there had been headache, vomiting and apathy, these symptoms having increased in severity to the date of patient's entrance to the hospital. The physical examination on admission revealed typical signs of meningitis, apathy alternating with irritability, rigidity of the neck, scattered petechiae, Macewen, Kernig and Brudzinski signs, a tache cérébrale and a moderate temperature. Lumbar puncture revealed cloudy fluid which was under considerably increased pressure and which showed the meningococcus in smears and cultures. Flexner's serum promptly introduced into the spinal canal failed to result beneficially, and instead of a rapid recovery, as was expected, the symptoms continued unabated for about a month in spite of repeated injections, given almost daily for the first week, then somewhat less frequently. The temperature remained septic in type; the restlessness, headache and signs of spinal irritability continued as on admission, and the spinal fluid at each puncture showed the meningococcus. At the end of four weeks the child's condition began to improve and kept steadily becoming better until the patient was finally discharged well, fifty-eight days after admission. The last culture of the spinal fluid, taken twenty-six days before discharge, still contained meningococci.

CASE 2.—J. H., aged 7½. The onset of this case was sudden, four days before admission, the child having complained of very severe headache and

pains in the neck and back. The patient had vomited several times and had had high fever. Physical examination showed the usual manifestations of meningitis—irritability, tache, Kernig, Babinski and Brudzinski signs and a petechial rash. On lumbar puncture 35 c.c. of cloudy fluid was withdrawn and found to contain the meningococcus. The fluid withdrawn at the third puncture, that is, after two injections of the Flexner serum, showed no meningococci in smears and in culture mediums. The symptoms, however, continued for five weeks. Repeated lumbar punctures were made, and although the fluid was always reported sterile after the second injection, the antimeningitis serum was injected on several occasions. The patient recovered after a protracted illness of nearly sixteen weeks.

It is interesting to note that these two refractory cases of meningococcus meningitis came from the same neighborhood, were infected at about the same period of time and failed to react to repeated injections of the antimeningitis serum.

To combat effectively these refractory cases illustrated by the above abstracts, it might be wise to culture the various strains of meningococci and to establish a "fast" antimeningitis serum to be used only in this type of infection, just as Dopter has prepared and used his antiparameningococcus serum; so that by this means we may eventually hope for a still greater diminution in the mortality of meningococcus meningitis.

30 West Eighty-Eighth Street.

CLINICAL DEPARTMENT

PERSISTENT VOMITING ASSOCIATED WITH "RUMINATION" IN AN INFANT OF FIVE MONTHS

FREDERIC H. BARTLETT, M.D.

Assistant Attending Physician to the Babies' Hospital

NEW YORK

A "vomiting baby" presents as many baffling problems as any condition in infancy. It is too often assumed that vomiting is a natural process and that it is only necessary to bide one's time and the baby will outgrow it. As a result of this attitude of mind, efforts at determining a cause of the vomiting are relaxed, matters are allowed to drift along, and medicines are given to satisfy one's conscience and to appease the family.

The most common causes of vomiting in infancy are connected with improper food and incorrect methods of feeding. A careful adaptation of the food to the child's tolerance or a proper regulation of the intervals of feeding and the amount of food in twenty-four hours will as a rule meet the indications in such cases. The question may reasonably be asked: How may "such cases" be determined? The obvious answer is: By a careful study and observation of the case under consideration. Too little attention is paid to the investigation of the conditions with which vomiting in infancy is related. Pitiful examples of this fact are seen in the cases of pyloric stenosis which are brought to the hospitals.

The following history represents an instance of vomiting connected with an unusual condition. The case is of sufficient interest on account of its rarity and of the results of treatment to warrant its being reported:

The baby was first seen on Oct. 1, 1913, when it was $5\frac{1}{2}$ months old. It was a first child, full term, and a difficult forceps delivery. The weight at birth was $8\frac{3}{4}$ pounds. At 2 weeks of age the weight was $8\frac{1}{4}$ pounds, and at 5 months 8 pounds. She was breast-fed for four weeks. The mother was then taken ill and breast-feedings were stopped. On the breast the child gave no symptoms of vomiting until the end of the third week. During the fifth week she vomited after every bottle. The vomiting was not projectile in character.

The first artificial food, which was begun at four weeks of age, was: milk 6 ounces taken from the top 12 ounces of a quart; water 22 ounces; milk-sugar 7 teaspoonfuls; milk of magnesia 1 teaspoonful— $2\frac{1}{2}$ to 3 ounces every two hours. On this mixture, vomiting took place after every bottle. The bowels were constipated. This food was continued for three months.

The second food was condensed milk 1 part, water 8 parts. This was tried for three weeks. The vomiting improved somewhat. This food was stopped on account of an acute attack of indigestion.

The third food was peptonized milk. This was begun at four months of age. It was prepared as follows: milk 16 ounces, water 16 ounces, and a peptonizing powder was added. Vomiting continued on this mixture after every feeding.

The fourth food was malted milk, which was being given when the child was first seen. This was begun one week after the child was 5 months old. It was prepared as follows: malted milk three teaspoonfuls to 5½ ounces of water. The baby was fed every three hours and given 4 ounces of this mixture at each feeding. The vomiting was less for the first four days, but for three days past had occurred after every bottle. The bowels were constipated on this. The baby was hungry after each of its feedings.

The physical examination showed nothing abnormal, except that the baby was much emaciated. The abdomen was watched for peristaltic waves, but no waves were seen. The child was vigorous in spite of its poor nutrition.

No adequate explanation for the persistent vomiting was determined at the first visit. The case was regarded as one of gastric indigestion and a food low in fat was prescribed, and the intervals of feeding were increased from two and one-half to three hours. The mother was instructed not to handle the baby after feeding and to feed her at regular times. The child was put on a skimmed-milk mixture, made up as follows: skimmed milk 18 ounces, obtained by removing 4 ounces of cream from the top of a quart; barley-water 14 ounces; lime-water 2 ounces; cane-sugar 2 tablespoonfuls. Of this mixture, 5 ounces every three hours and six feedings a day were advised. The barley-water was made by adding a tablespoonful of barley flour to one pint of water and cooking the mixture for twenty minutes.

October 16 weight was 8 pounds. The vomiting showed no improvement on the skimmed-milk mixture. The baby was watched while taking its bottle, and the following phenomenon was noted. After finishing the feeding the baby began a suction motion with its tongue. She pushed out the tongue between the lips and drew it back again. This was repeated for ten or fifteen minutes. With each projection of the tongue between the lips milk came into the baby's mouth. She would swallow the mouthful and pump more out of the stomach. From time to time a large quantity would be drawn into the mouth and flow between the lips. This constituted the vomiting. The mother had noted this tongue-action from the time the baby was 4 months old and volunteered the information that she had often compared it to a cow chewing her cud. From the mother's statement and from the observation of the child, the descriptive word "rumination" fitted the phenomenon. At this date the baby was put on a mixture made up as follows: barley flour four tablespoonfuls, and milk one quart. This was to be cooked two hours in a double boiler. Of this mixture four tablespoonfuls were to be given every four hours, five feedings a day. After cooking, this mixture made up about one quart of food. After it was heated to feed to the baby, it was of the consistency of condensed milk. It was fed with a spoon. The baby was offered water between feedings and would take an ounce or two at a time. It is an interesting fact that the baby retained this without any evidence of the tongue-suction which followed the milk feedings.

October 23, the mother reported that the vomiting was less than on the skimmed milk. The mixture was changed by increasing the barley flour to six tablespoonfuls, which was added to one quart of milk. The object of the mixture was to obtain a food of such consistency that the baby could not pump it out of the stomach. Four tablespoonfuls of this were to be given every four hours, five feedings a day.

November 10, weight was 12 pounds. The baby had gained four pounds in three weeks. The vomiting and rumination stopped entirely as soon as the food was made up with six tablespoonfuls of barley flour to a quart of milk. The stools were three to four a day and were yellow, smooth and semi-formed. The baby was happy all the time and slept from 6:30 p. m. to

5:30 the next morning. She was getting four feedings a day of six tablespoonfuls at a feeding. The hours of feeding were 6 and 10 a. m., and 2 and 6 p. m.

November 24, weight was 12¾ pounds. One week ago she refused the food entirely for three days. She was not urged to eat and her appetite returned promptly. The vomiting and tongue-suction had not returned. There was now noted craniotabes of the right and left parietal bones.

One-half the yolk of a hard-boiled egg, mixed with the amount of barley-milk given at the 2 p. m. feeding, was added to the diet. The egg was to be boiled twenty-five minutes. One ounce of orange-juice was to be given at 8 a. m. The formula for making the gruel was now as follows: milk, 1½ quarts; barley flour, nine tablespoonfuls. The whole was cooked for two hours in a double boiler. Four tablespoonfuls of this mixture was given every four hours, at 6 and 10 a. m., and 2 and 6 p. m.

Feb. 18, 1914, at the age of 10 months the baby weighed 19 pounds and 14 ounces, net; head, 17½ inches; anterior fontanelle, 1¾ inches. Craniotabes of both parietal bones was still present. There were no other signs of rickets, except a rather prominent abdomen. The vomiting and tongue-suction had not returned. The child was very vigorous, slept well and was happy.

June 10, the mother reported that the child, aged 13 months, weighed 23¾ pounds, net. This was a gain of 15¾ pounds in seven months. There were five teeth. The child was sitting alone and trying to creep. She said a few single words, such as "dada," "mama," "kittie," etc. Her appetite was satisfied. She was having two stools a day. There had been no vomiting and tongue-sucking since October 16. The baby slept from 6 p. m. to 6 a. m. She was a happy, merry child, and seldom cried. She would often sleep from 10 until 2 o'clock in the daytime.

The following régime had been in effect for three months:

6 a. m.: Milk gruel, three tablespoonfuls.

8 a. m.: Orange-juice 2 ounces.

10 a. m.: Milk gruel, three tablespoonfuls; yolk of hard-boiled egg or cooked cereal (three tablespoonfuls). The cereal was taken without the addition of milk.

2 p. m.: Milk gruel, three tablespoonfuls; spinach, two tablespoonfuls; beef juice, 1 ounce with bread-crumbs.

6 p. m.: Milk gruel, three tablespoonfuls; yolk of hard-boiled egg.

The milk gruel was made as follows: whole milk, one quart; barley flour, five tablespoonfuls. This mixture was cooked in a double boiler for two hours. The spinach was cooked two hours and then rubbed through a fine sieve. The baby drank at least a glass (8 ounces) of water in twenty-four hours.

DISCUSSION

1. The vomiting in this case was apparently due to a peculiar suction-action of the tongue. The phenomenon may best be compared to that of a cow chewing its cud. The descriptive word "rumination" applies more closely than any other to this phenomenon. The consistency of the milk gruel was compared to that of glue. The question arises as to whether food of this peculiar character presented mechanical difficulties to its being pumped out of the stomach.

2. This is one illustrative instance of the tolerance of a 5-months-old baby for starch. No deduction is to be made from this single experience that all babies of this age can tolerate as large a quantity

of starch as did this baby. At the same time, there is good reason to believe that young babies can tolerate larger quantities of starch than have heretofore been given.

3. This baby tolerated a mixed diet of egg, cereal, fruit and green vegetables after 8 months of age. There was evidence of beginning rickets, which showed a decided retrogression after the mixed diet was begun. This suggests the advisability of introducing solid food into the dietary of infants earlier than is usually the practice. This suggestion applies particularly to healthy children.

4. A wider application of this form of dietetic treatment is suggested in cases of vomiting. It is necessary to exclude organic causes for persistent vomiting, for example such as pyloric stenosis. It is also advised to try first such dietetic procedures as food with low fat, lengthening the intervals of feeding and avoidance of handling after feeding, but there are many cases of vomiting which persist in spite of rational treatment. It is suggested that a trial be given of a food of the consistency which was given in the foregoing case. At what age may this food be tried? The patient in the case just cited was 5 months old. I have had no experience with it in babies younger than 5 months, but believe it may be applicable in younger babies.

44 East Sixty-Third Street.

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WEIGHTS AND MEASUREMENTS OF INFANTS AND CHILDREN IN PRIVATE PRACTICE COMPARED WITH INSTITUTION CHILDREN AND SCHOOLCHILDREN *

ROWLAND G. FREEMAN, M.D.
NEW YORK

Information as to the weights and measurements of children is only beginning to be reliable. Much that is erroneous has been published concerning the weights during the first year and very little data has been published as to the gain in weight and height of children under the good conditions that usually prevail in the feeding practice of pediatricians.

While believing that standard weight charts are an absolute disadvantage when given to the family, there can be no question but that a physician feeding a baby should have certain standards in mind, although each baby will supply a standard of its own.

While most of us have the care of a considerable number of children under very good conditions where the feeding can be, at least during the first years, absolutely controlled, where the exposure to fresh air, the amount of exercise, the amount of rest and the character of the clothing are all supervised, we have had little definite knowledge as to whether the results obtained for these children were commensurate with the care that was given them. We know in a general way that the mortality of these children is much less than that of children in general. For while the mortality in New York during the first year, which was, some years ago, 30 per cent., is now about 10 per cent., I believe the mortality for well-cared-for babies during that period to be not more than one-half of 1 per cent. Of this fact again we have no definite data, but of the 120 consecutive cases in private practice that I have tabulated, not one died during the first year.

There has been accumulated now a considerable number of weights and measurements of schoolchildren in the United States, while the only data that I know of the weights and measurements of children in

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private practice are those published by W. Camerer.¹ It therefore seemed of interest to me to make an average weight chart of 278 cases in private practice, as well as a chart showing their measurements, and in order to get definite data for comparison I weighed and measured the 1,000 children, about 500 girls and 500 boys, in the Roman Catholic Orphan Asylums of New York. These institutions are now situated on a high bluff overlooking the Harlem River, with modern, sanitary buildings, well lighted and with ample grounds, so that while these children are institution children they are really under good conditions, and there was almost no sickness among them at the time I made these observations.

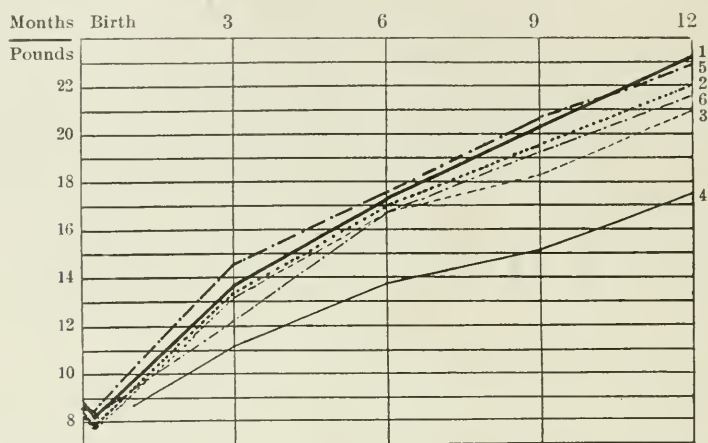


Chart 1.—Weight during the first year of 120 well-cared-for children (1), compared with the average given by Dr. Holt (2 and 3) that of 500 institution children (4); that given by Dr. Camerer for 119 breast-fed children (5), and 84 artificially fed children (6) in private practice.

I have prepared several charts in which I have compared the weights and measurements of the children in private practice, the orphan asylum children, and such data as I have obtained from other observations.

Chart 1 shows in the heavy black line the weights of 120 well-cared-for children, consecutive cases in my private practice, while the light line shows in contrast the average weight during the first year of 500 institution children.² It is noticed that these lines are well separated after the first month. The dotted lines which run well below the well-cared-for children, are taken from the different editions

1. Camerer, W.: *Jahrb. f. Kinderh.*, 1901, lii, 381.

2. Fleischner, E. C.: *Arch. Pediat.*, 1906, xxii, 740.

of Dr. Holt's book.³ The lower line is the one used in the earlier edition (Second Edition, 1902) and "is made up from complete weight charts of 100 healthy nursing infants who were thriving and weighed every week, and the incomplete charts of about 300 other infants"; while the upper one is the one used in the last edition (Sixth Edition, 1911) and is made up from observations on the same number of children as the lower line. Both of these lines are seen to be below the well-cared-for children. The two dot and dash lines are the weights published by Camerer, the upper line representing breast-fed children and the lower line the artificially fed children. The breast-fed children show greater weight throughout the first nine months, while the artificially fed children keep fairly below. I may add that the 120 well-

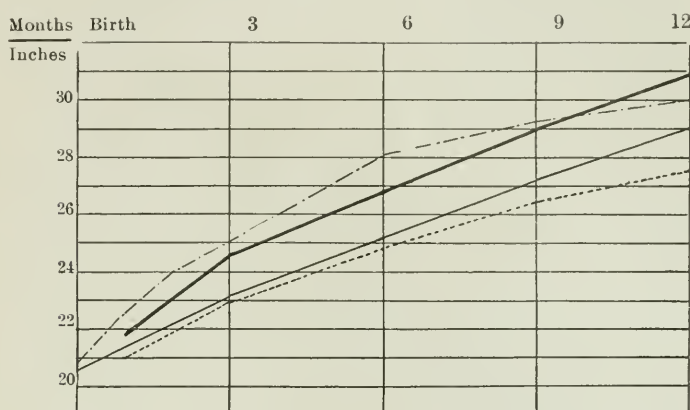


Chart 2.—Height during the first year of 120 well-cared-for children ————— compared with the average given by Dr. Holt ———, that of 500 institution children and that of 34 children given by Camerer — — — —.

cared-for children represented in the chart were almost entirely artificially fed after the first month, so that the American method of feeding children during the first year would seem to compare favorably with the method advocated in Germany.

Passing to Chart 2, we have in the heavy black line, again, the length of the same 120 well-cared-for babies that are represented in the other chart, while the lower, dotted line represents the measurements of the 500 institution children, and the light black line is the line taken from Dr. Holt's book, while the dot and dash line represents the measurements of thirty-four children reported by Camerer with no information as to whether they are breast fed or artificially fed. His line, however, corresponds to that of the breast-fed babies in the weight chart, being

3. Holt, L. E.: Diseases of Infancy and Childhood.

above my line at the first nine months and ending below it. It must, however, be considered that the thirty-four cases reported by Camerer are an insufficient number for the formation of conclusions, as there are only one to five observations on any given date.

The observations on children after the first year are represented in Charts 3 and 4.

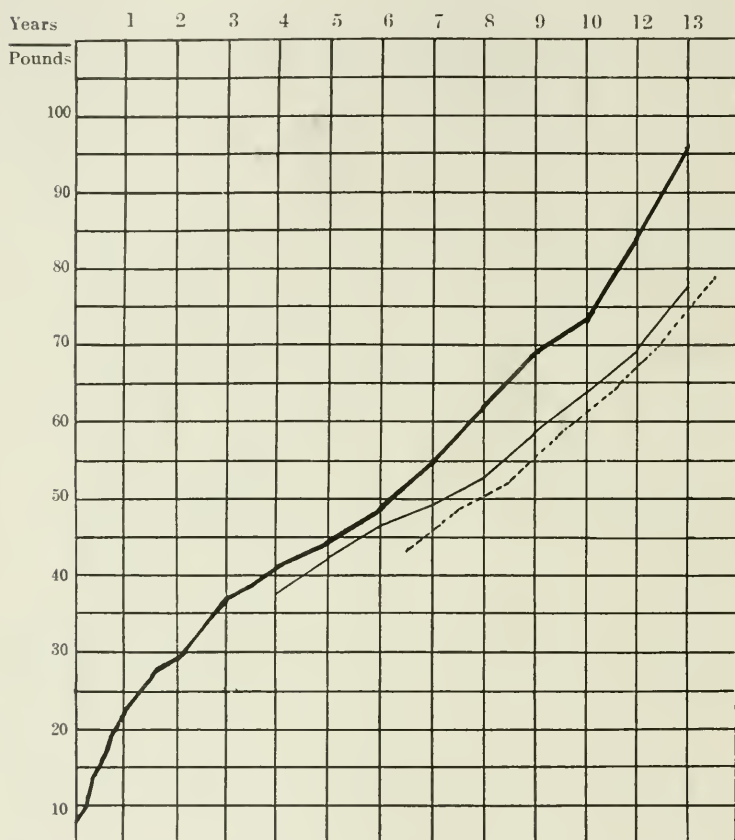


Chart 3.—Weight in pounds of 278 well-cared-for children ————— compared with 1,000 orphan asylum children ——— and 69,000 schoolchildren - - - - -.

Chart 3 shows in the heavy black line the weight of 278 children in private practice as compared with the 1,000 orphan asylum children in the light black line, and with 69,000 schoolchildren in the dotted line, of various cities of the United States, as reported by Stanley Hall. It is noticeable that while from the fourth to the sixth year the orphan asylum children average two or three pounds less than mine, these lines

become farther apart with advancing age. It is an evidence of the excellent care given these orphan asylum children that they average 2 or 3 pounds heavier than the 69,000 schoolchildren. Both of these groups, however, from 6 years on, are well below the well-cared-for after several visits from a social worker, the child was not brought cared-for children.

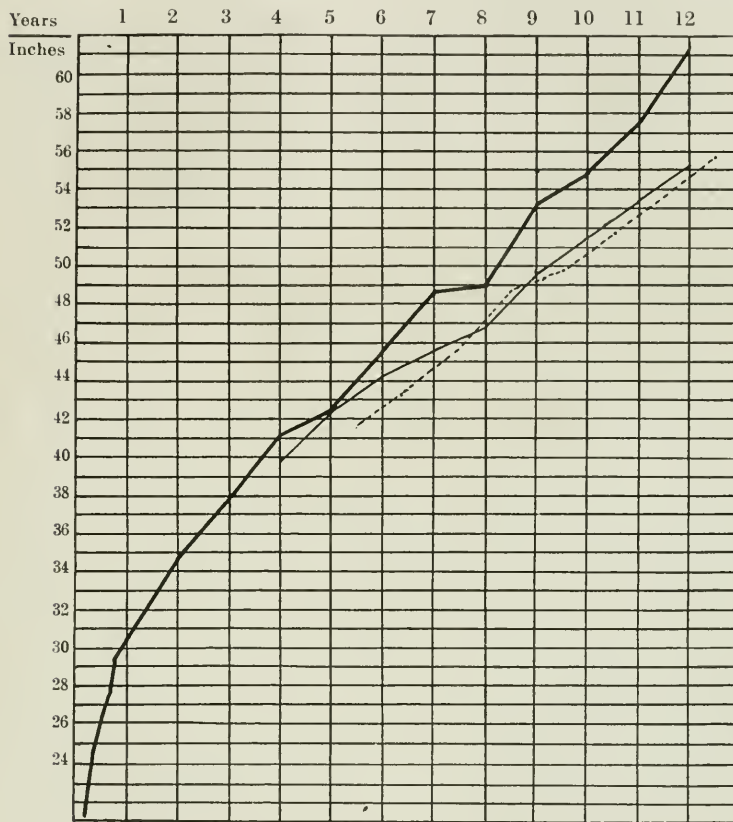


Chart 4.—Height in inches of 278 well-cared-for children — compared with 1,000 orphan asylum children — and 98,000 schoolchildren - - - -.

The last, Chart 4, which represents the length of the 278 well-cared-for children in the heavy line as compared with the 1,000 orphan asylum children in the light line, and 98,000 schoolchildren of the United States as reported by Stanley Hall, in the dotted line, shows the orphan asylum children again to average somewhat taller than the schoolchildren, both lines being well below the well-cared-for children. This shows a surprising advantage of the well-cared-for children over the others at the twelfth year, of 6 inches greater height.

In conclusion, I would say that the children that are under good control so far as diet, rest and exercise are concerned, show a great advantage over the data at hand concerning other children both in weight and height during the first twelve years of life; and that at the twelfth year they surpass the average by 20 pounds in weight and 6 inches in height.

211 West Fifty-Seventh Street.

HEREDITARY SYPHILIS AS A SOCIAL PROBLEM *

P. C. JEANS, M.D., AND ELSA M. BUTLER, A.M.
ST. LOUIS

In a busy and overcrowded clinic, where only the most obvious and pressing needs can be seen at a glance, it is much easier to give the individual patient the immediate care which he needs than to grasp and classify the multifarious problems which the patients as a whole present. By watching and weighing these problems, in the course of time it became clear that the luetic children who were attending the various clinics in the St. Louis Children's Hospital presented a serious medical and social problem out of all proportion to their numbers in the clinics. It was noticed that many of the luetic children were brought to the clinic for a short period only. Some never returned after the initial visit. Others were brought until the immediate symptoms were cleared up and then were lost track of completely. This waste effort brought to the attention of the physicians the need of constructive work.

It is obvious that the medical side of the problem was untouched in the case of the patients needing care who did not return to the clinic. Therefore in the fall of 1913 the assistance of the Social Service Department was actively enlisted to bridge the hiatus between the dispensary and the homes.

In those cases in which the apparent manifestations had been cured, it was necessary to make a special point of explaining to the parents the property of this disease to become latent, and later to manifest itself in some disagreeable or even fatal form and prevail on them to continue the treatment. It was further necessary to examine the other members of the family represented and treat the affected children. It was also necessary to urge the treatment of the affected parents.

It seemed that no part of this program could be omitted if our work was to be efficient; and it was our opinion that the complete working out of the part of this community problem which presented itself to us was a part of the hospital's debt to the community.

When the children were being brought to the clinic regularly, the program outlined above was of course handled by the physicians alone, since the treatment is a purely medical problem. Three types of cases were, however, referred to the Social Service Department:

* Submitted for publication June 20, 1914.

* From the St. Louis Children's Hospital.

1. Children who were known to be luetic and whose parents, through ignorance or indifference failed to keep up the treatment or to report at the proper intervals.

2. Children who had clinical evidence of the presence of syphilis and therefore needed to have Wassermann tests made to verify the diagnosis, but failed to return for the Wassermann test.

3. Brothers and sisters of the patients whom the parents could not or would not bring for examination and for Wassermann tests.

1. The first group represents the greatest number of offenders. Because of the quick response to treatment in case of the acute manifestations of syphilis, the interest of the parents, which was at first perhaps intense, is apt to die out simultaneously with the disappearance of the acute symptoms. He will insist that the child is well, which to all outward appearances he may be; or he may state that returning for treatment involves too great an expenditure of time and trouble. Only when permanent damage has already been done, will he begin to realize his parental responsibility. It sometimes happens, even in an evidently uncured case, that the shock of initial revelation wears off, and the parent neglects to continue the treatment.

A good example of this state of affairs may be seen in the case of W. B. As an infant he had a rash which responded promptly to mercurial treatment, which was then stopped. At 6 years he developed an interstitial keratitis and was under the constant care of a physician for one year, when he recovered. Again treatment was discontinued. At 9 years he developed cerebrospinal manifestations, with epilepsy. This was allowed to go untreated, until he was brought to the Children's Hospital at 11 years of age. At this time he was brought for a burn and not for his other condition. He was treated for syphilis while in the hospital with considerable improvement. When his burn was well, he was discharged, to be treated in the dispensary. After discharge, the mother refused to bring him back, saying he was in the country, and, in her opinion, well. She also refused to cooperate by bringing in the other children for examination. A short time ago she returned with a younger child who showed evidence of syphilis of the nervous system. At this time the whole situation was again explained to her, and she promised to cooperate in every way possible, but at this writing she has not been back with any of the children, not even with the sick ones. Other cases equally flagrant might be cited.

After parents understood why treatment was necessary, the children were usually brought back. There were, however, some parents with whom indifference or the desire of shielding themselves outweighed the importance of treatment. It soon became clear that persuasion alone in these cases was not productive of results, so the sup-

port of the Juvenile Court was enlisted, on the ground that syphilitic children not under treatment, could be brought into court as "neglected children."

The court has taken the stand that the parents must give satisfactory evidence that the luetic child is being treated, but the parent has the option of returning to the original clinic where diagnosis was made, or going to another clinic, or securing the services of a private physician. Out of the whole series studied, only eleven were referred to court.

At no time were the parents threatened with court procedure. If, after several visits from a social worker, the child was not brought back, the Juvenile Court was notified. An officer of the court then went to the home and explained in a friendly way that unless the child was treated the parents would be brought into court. In every case but one such timely advice sufficed. The parents quickly saw that treatment would in any case be enforced, and that it was far easier to acquiesce than to have the nature of the child's malady publicly stated in court.

The results accomplished through court cooperation have been most interesting.

TYPES OF COURT CASES

1. M. G. was a girl of 6, who had come originally because she was suffering from spastic paralysis. In June, 1913, a Wassermann test was made, which proved positive. Many calls were made to induce Mrs. G. to bring M. to the clinic, but without success. Finally, through an order from the chief probation officer, M. was brought to the hospital by a social worker and treated for one week. At the end of that time, the mother insisted on removing M. from the hospital. She was forced to bring to court a written statement from a physician that he would treat M. and not discontinue treatment without reporting to court. This physician was anxious to assist in every way. He made several visits to the hospital to learn what treatment had been used. In the course of six weeks, this same physician returned with request that M. be treated in the clinic with neosalvarsan at his own expense.

As has been stated, when parents presented satisfactory evidence that child was under care of a private physician, no further steps were taken to follow up the case, since in the opinion of the Court a parent has the right to choose his own physician. But in cases in which the bare statement was made that child was being treated it was felt that the Juvenile Court should take the responsibility of placing the burden of proof on the parents.

2. An interesting example of this was a boy, E. F. E. F. came to the clinic in November, 1913, and a Wassermann test was made, which proved positive. E. F. came back five times quite regularly for treatment, and then stopped. Since E. did not return, a visit was made to the home, to learn the cause for his remaining away from the clinic. Mr. F. stated that he was prescribing for E. himself, giving him caffein and Scott's Emulsion, and refused to have E. treated by a physician.

Since persuasion was futile, the case was referred to the Juvenile Court. Mr. F. was required to bring a written statement to court from a doctor, stating that E was under his care.

3. V. R. was a colored child about 27 months of age and to all appearances perfectly well. In June, 1913, a positive Wassermann reaction was obtained. The mother was visited repeatedly from October until April, but always gave as an excuse for not returning that she disliked seeing so many sick children, and came away from the clinic greatly distressed. Although the mother was an ignorant, unmarried girl, she managed to thwart all procedure from June, 1913, until April, 1914, when she was forced by court to have V. treated.

As a test case in court, V. R. was considered peculiarly interesting, since she had no clinical manifestations of syphilis. That a judge was able to grasp the importance of the problem and willing to take such an advanced stand, speaks well for the general future effectiveness of the Juvenile Court.

2. In the second group of cases—in which a clinical diagnosis of syphilis is made, but the patient fails to return for a Wassermann—we have relied almost altogether on persuasion, since it has happened in many of these cases that the clinical evidence alone without the Wassermann test did not seem sufficient proof to refer to the Court.

3. In the third group—the examination of the other children of the family—there has been a fairly ready response on the part of many of the parents. In this regard a further step in court cooperation has just been secured. Hereafter in any family in which a child is found to have an hereditary syphilitic infection, if necessary, court authority will be used to force the parents to have the rest of the children examined.

In the case of the parents our difficulties are at present apparently insurmountable. There have been a few who have gone willingly on our advice to some physician or clinic for treatment. For the remainder we can do nothing but explain and persuade. We can only let them continue their possible additions to mortality in real and potential life or to the asylum population of the community.

We realize that the enforced examination and treatment of patients is condemned by some, and that this broader view of the problem might be considered as outside the province of a hospital clinic, but in our opinion it is a legitimate work and duty which the hospital owes to the community. The Children's Hospital has been established in part to recognize community problems and in so far as possible to be an intelligent leader in directing their solution. Since the hospital was touching the social problem represented by syphilis it was felt that in order to get a real knowledge of the magnitude and character of the problem in St. Louis, an intensive study should be made wherever possible of the conditions to be found in the community at large. Therefore some of the social aspects of a group of cases of hereditary

syphilis at the St. Louis Children's Hospital together with data obtained elsewhere in St. Louis seem of sufficient interest to be presented.

ILLEGITIMACY

In studying the relation of hereditary syphilis to illegitimacy, very few definite data can be obtained. The only comparisons we have been able to make have been based on the infant death statistics of St. Louis for 1913 (Table 1).

TABLE 1.—STUDY OF CONGENITAL SYPHILIS, IN ITS RELATION TO ILLEGITIMACY

Of all deaths in infants in St. Louis in 1913.....10 per cent. were illegitimate
Of all deaths in infants due to syphilis.....15 per cent. were illegitimate
Of the deaths in our Group 1.....22 per cent. were illegitimate
(Group 1 consists of all luetic infants belonging to the Children's Hospital series).

This shows that the mortality is much higher among syphilitic illegitimate infants than among illegitimate infants in general (Table 2).

TABLE 2.—DEATHS DUE TO SYPHILIS (St. Louis, 1913)

Type of birth	Percentage		
	Total	Legitimate	Illegitimate
Living	3.5	3.0	5.1
Still	2.9	2.7	5.0

Among both living births and still-births syphilis was present in a larger proportion of the illegitimate than the legitimate children.

COLOR

That there is a difference in the morals and the standards of living between the negroes and the whites is well known. And since syphilis is a disease which is engendered and spread by low standards of living and morals, it has been interesting to see whether in the groups studied the frequency of the disease has any relation to color.

We find that syphilis is diagnosed in 2.5 per cent. of our clinic patients. It occurs 2.5 times more frequently in the colored than the white patients, 2.2 per cent. of the whites being syphilitic and 5.5 per cent. of the colored. White patients represented 92 per cent. of our clinic attendance, but only 83 per cent. of our syphilitics. Colored patients represented 8 per cent. of our attendance and 17 per cent. of our syphilitics.

In studying the St. Louis vital statistics for 1913, we find syphilis given as a cause for still-births twice as frequently in colored as in whites, while for infants who were born alive, but who later died, syphilis is given as a cause of death 3.5 times as often in colored as in whites.

INCIDENCE AND MORTALITY

During 1913 in the out-patient department of the Children's Hospital a total of 5,185 new patients were treated. Of these, 108, or 2 per cent. had congenital syphilis. But by separating these 5,185 into two groups — (1) children under 13 months; (2) children 13 months of age and over — we find a wide difference in the proportion of syphilitic children in these two groups, as is shown by Table 3.

TABLE 3.—COMPARISON OF CHILDREN UNDER AND OVER 13 MONTHS WITH RESPECT TO SYPHILIS

Group	Total	Syphilitic	Per Cent. Syphilitic
1	854	42	4.9
2	4,331	66	1.5

The difference in the two groups is probably due to two facts — (1) a large number of infants infected with syphilis die; (2) as a child grows older the more acute symptoms are not so likely to be manifest, so that many cases of latent syphilis pass by unnoticed.

In discussing hereditary syphilis, incidence and mortality are so closely interwoven that it seems appropriate next to show the high proportion of deaths among children of luetic parents. For a basis of comparison, a study has been made of the families represented by the syphilitic children, one hundred families represented by children treated in the hospital for contagious disease, and one hundred families represented by children taken at random from the hospital records. The syphilitic families for whom we have data number eighty-three. For convenience, these groups will be called S, C and R, respectively (Table 4).

TABLE 4.—MORTALITY AMONG THE VARIOUS GROUPS

Group	Total Children Born	Total Children Dead	Per Cent. Dead
S	270	66	30
C	398	70	17
R	400	59	15

In other words, the mortality among the children in the syphilitic group was practically twice as great as that of either of the others. Now 15 per cent. and 17 per cent. represent what is at present to be found in the average poor family. What explanation can be found for the 30 per cent. in the syphilitic group except the damage caused by syphilis, since the families studied came from the same stratum of life, made up of people of the same standards of living, the same intelligence and training, the same income and living in the same neighborhoods?

Turning now to a broader field we may consider syphilis in its bearing on infant mortality as revealed by the St. Louis vital statistics

of 1913. During 1913 there were 14,958 births recorded. Of this number, 711, or nearly 5 per cent., were still-births. Twenty-one still-births, or 2.9 per cent. of all stillbirths, were due to congenital syphilis. That this figure must greatly underestimate actual conditions can be seen by examining the records of the Obstetrical Department of the Washington University Hospital. From Jan. 1, 1913, to Jan. 1, 1914, 565 women were cared for during parturition. There were 40 still-births, of which 16, or 40 per cent., were known to have been caused by syphilis, since an autopsy had been made in each case. A few others were probably syphilitic, but the diagnosis was not confirmed by autopsy.

TABLE 5.—COMPARATIVE STUDY IN DESTRUCTION IN LIFE DUE TO SYPHILIS

Families Represented by	Total Pregnancies	Miscarriages	Premature Births	Still Births	Dead Among Living Births	Total Waste	Per Cent. Waste
100 R	442	31	6	5	59	101	25
100 C	444	39	2	5	70	116	26
83 S	453	84	10	22	104	220	46

(Figures for "S" calculated to 100 families.)

In the city of St. Louis there were 14,247 living births recorded in 1913, and 1,469 deaths occurred in this group. Fifty-two of these deaths, or 3.5 per cent., were recorded as due in whole or in part to hereditary syphilis. The error in this figure is probably not so great as in the stillbirths, but here also one feels that the figure is low, partly because of a general dislike of stating syphilis as a cause of death. Especially is this true with private physicians as compared to physicians in public institutions. This may be indicated by the fact that, though only 25 per cent. of all deaths in 1913 in infants occurred in hospitals, 50 per cent. of all diagnoses of congenital syphilis as a cause of death were given for babies who died in hospitals.

In studying the family conditions revealed by the birth and death certificates we find that in the families represented by infants which were born alive, but which later died of syphilis, 59 per cent. of all the children born in these families are now dead. In the families represented by the stillbirths due to syphilis 81 per cent. of all the children born are now dead.

Since damage wrought by syphilis must not be confined to study of living children alone, we compared the three groups of cases C, R and S, enumerated above to see just how important and destructive a factor syphilis has been in the total waste of human life.

Thus it is seen that the waste of life is almost twice as great among children of syphilitic families as among similar families that are not syphilitic.

In further study of the damage caused by hereditary syphilis we wish to call attention to the high mortality in our Group 1 and the high morbidity in Group 2.

Among the children under 13 months in the group still under study, eleven, or 22 per cent., have already died before reaching the age of 1 year. That more in this group will die at an early date seems at present apparent. The general mortality rate for infants in St. Louis is about 10.3 per cent.

Of the 74 children in Group 2, twenty-five show permanent and fourteen show long-continued temporary damage. These figures include only the disabling manifestations. The cases of permanent defect were all affections of the nervous system, and the cases of long-continued temporary damage all affections of the eye. Some of these eye affections have been faithfully under treatment for nearly two years, and though greatly improved, the vision is still impaired.

It is of interest in this connection to compare the amount of feeble-mindedness in the three groups R, C and S (Table 6).

TABLE 6.—PREVALENCE OF FEEBLE-MINDEDNESS

Group	No. of Families	Families with Defectives	Per Cent.
S	83	17	20
C	100	4	4
R	100	3	3

It would seem that there is five times as much feeble-mindedness in the syphilitic group as in the non-syphilitic families. It is easily possible, however, that there is a fallacy in this compilation, in that mothers in giving their family history will not always disclose the fact that they have defective children.

VALUE OF MATERNAL NURSING

The fact that breast feeding is the greatest preventive force in curtailing infant mortality is well known. Yet it is important to state such a well established fact, since the nature of the feeding plays an even more important part in the chance for life among syphilitic than among non-syphilitic infants.

During the time that the intensive study of syphilis has been carried on, forty-nine infants have been treated. Eleven of these have died, representing a mortality of 22 per cent. Of the eleven infants who have died, ten, or 88 per cent., were artificially fed.

Of the 49 infants in Group 1, the character of feeding is known in case of 30; of these, 19 were artificially fed, and 11 were breast fed. Of the 19 artificially fed babies, 10 have already died. Of the 11

breast-fed babies one has died. None of these deaths was due to summer or diarrheal disturbance, but largely due to malnutrition as a result of syphilitic infection.

In the older group of children there were 27, the character of whose feeding in infancy is known. Of these, 4, or 15 per cent., were artificially fed. In order to get some estimate of the relative amount of breast and artificial feeding in general in the class of patients represented by the group under study, the hospital records of older children show that about 28 per cent. had been artificially fed in infancy. Though perhaps no definite conclusion can be drawn from this, it is very significant that with probably the same prevalence of artificial feeding in infancy almost twice as many of the non-syphilitic children survived on artificial feeding as did syphilitic children.

SUMMARY

As a social problem, hereditary syphilis assumes relatively large proportions, one patient often representing a number of individuals needing treatment.

Parents are frequently indifferent and fail to continue treatment. They also frequently fail to see the importance of having Wassermann tests made on the other children of the family, who may seem perfectly well, but who may have syphilis. In the case of such parental indifference such tests or treatment should be enforced.

Hereditary syphilis is more frequent in illegitimate than legitimate children.

The mortality is higher in illegitimate syphilitic infants than legitimate syphilitic infants.

Hereditary syphilis in St. Louis is from two three times as frequent in the colored as in the white race.

The frequency of hereditary syphilis is greater among the infants in our clinic than among the older children.

The waste in potential life by miscarriages and deaths in syphilitic families is twice as great as in non-syphilitic children.

Thirty-three per cent. of the syphilitic children over one year had permanent disabling damage. Eighteen per cent. of the syphilitic children over one year had long-continued temporary disabling damage.

There is about five times as much feeble-mindedness in syphilitic families as in non-syphilitic families.

The mortality for artificially fed syphilitic infants is five times as high as for breast-fed syphilitic infants, not including deaths due to intestinal disturbances.

We are indebted to the College Club of St. Louis for access to their work on the St. Louis vital statistics.

St. Louis Children's Hospital.

SPLENOHEPATOMEGALY GAUCHER

MARK S. REUBEN, M.D.

NEW YORK

I have already¹ reported a case of splenomegaly Gaucher in a child 4 years old. In March, 1912, splenectomy was performed on this patient. The child did not survive the operation. Histologic study of the liver, the spleen, the lymph glands and the bone-marrow confirmed the diagnosis previously made on a clinical basis. This is the first case to be reported in the English language in which the diagnosis in a child was made prior to operation or to necropsy, and was confirmed later. The diagnosis was correctly made in a child only once before, by De Jong and Van Heukelom in 1909.

In the previous paper a study of this disease was presented as it occurs both in adults and in children. In this paper only the cases which occurred in infants and children will be discussed. Although the clinical picture is almost identical with that which occurs in adults, the course of the disease and the indications for treatment are so different that it seems best not to include in this study, the cases reported in adults. Since the publication of the previous article, three other cases of this disease in children were reported; in all of these the diagnosis was made after splenectomy.

REPORT OF CASES

Family History.—Father and mother both living and well; there is no tuberculosis in the family; nor could any luetic history be obtained. The mother has given birth to four children, and has had no miscarriages nor stillbirths. Anna, the oldest child, is 11 years old. Lilly died in 1909 at the age of 8; Freda is 9 years old, and Max, the youngest, is 4 years old. Wassermann reaction of mother negative.

The boy came to my notice at the Vanderbilt Clinic June 10, 1911, where he was brought for treatment on account of a progressive enlargement of his abdomen. The mother stated that an older child (Lilly) had had a similar condition and that that child died two years previously; as this child (Lilly) had been at Mt. Sinai Hospital (1906) at a time when I was a member of the house staff of this hospital, I can recall the case very clearly. At the hospital no diagnosis was made. This child was also treated at the Vanderbilt Clinic in 1904, and notes of the case show that at that time the child had a much enlarged spleen and liver. No diagnosis was made at the time.

CASE 1.—Anna: Physical examination of this child revealed nothing abnormal; she was in good physical condition, the liver and spleen were not enlarged.

CASE 2.—Lilly: This child died two years previously at the age of 8; she had measles at 2 years; no other diseases of infancy; no history of malaria. At 4

1. Reuben, Mark S.: Splenomegaly (Gaucher), AM. JOUR. CHILD. DIS., January, 1912, p. 28.

years the child began to be troubled with enlargement of the abdomen; also complained of dragging sensation in the side and weakness. The abdomen was progressively increasing in size; at the time the child was at the hospital the liver was 10 cm. below the free border of the ribs, and the spleen was beyond the median line and well filled the left iliac cavity. The child had at no time any hemorrhages nor oozing from the gums, and there was no discoloration of the face.

The blood examination showed the following:

Red blood-cells, 3,440,000; white blood-cells, 6,200; hemoglobin, 68 per cent.; differential count, normal; no abnormal cells present.

Mixed treatment, arsenic and Roentgen ray were ineffectual and the child was discharged from the hospital unimproved. A few months later the child suddenly developed dyspnea and cyanosis and succumbed before a physician could be called.

CASE 3.—Freda: The third child was 9 years old; she had no diseases of infancy, and there was no history of malarial infection. During the last year she complained of pain in the abdomen. Physical examination showed the liver to be enlarged; the edge was palpable 2 inches below the free border of the ribs. The spleen was not enlarged and the edge was not palpable. The blood examination showed the following: Red blood-cells, 4,344,000; white blood-cells, 7,000; hemoglobin, 75 per cent.; differential count, normal; no abnormal cells present.

There was no pigmentation of the skin, and no history of any hemorrhages nor oozing from the gums or lips; there was no bone tenderness and the lymph-glands were not enlarged. Whether Freda was suffering from the same disease as Lilly and Max (the latter case to be described later) only the future will reveal, but she had a much enlarged liver, which cannot be attributed to any other cause; whether she will develop a large spleen later cannot be definitely stated.

CASE 4.—Max: The fourth child was a boy 4 years old; he had no diseases of infancy; he was not rachitic, and there was no history of malarial infection. About one year previously he was thrown down by a horse; at this time the attending physician told the mother that the child had a large liver and spleen; since that time the mother noted a progressive enlargement of the abdomen and brought the child to the clinic on that account. Examination of this child showed there was a distinct discoloration of the face; the color varied from light yellow to golden hue. The pigmentation was most marked at the bridge of the nose and around the eyes. There was no discoloration of the conjunctivae. There was a general languid appearance, and the child moved about very slowly; the child did not complain of any pain nor was any tenderness to be elicited in the chest or abdomen. Heart and lungs were normal. The liver was much enlarged and the edge was palpable at the umbilicus; there was no tenderness over the liver. The spleen reached to 2 inches below the umbilicus and extended over the median line to the right as far as the mammary line.

The blood examination showed the following: Red blood-cells, 2,208,000; white blood-cells, 5,000; hemoglobin, 35 per cent.; differential count, normal; no abnormal cells found. There was no history of hemorrhages; no bone tenderness, and the lymph-glands were not enlarged. Wassermann reaction negative.

Iron and arsenic were administered and other hygienic measures were instituted; under the treatment the child's condition and the blood-picture improved; but in spite of the general improvement, the spleen and the liver continued to enlarge; in view of the fatal termination of this disease in a sister of this patient, splenectomy was advised, and the child was referred to Mount Sinai Hospital for operation.

The blood examination at time of admission to the hospital was: red blood-cells, 4,000,000; leukocytes, 4,200; hemoglobin, 68 per cent.; color-index, 0.85;

differential count: polynuclears, 70 per cent.; large lymphocytes, 25 per cent.; small lymphocytes, 3 per cent.; mononuclears, 1 per cent.; myelocytes, 1 per cent.; no normoblasts; slight poikilocytosis and anisocytosis.

Splenectomy was performed by Dr. Joseph Wiener on March 1, 1912; the spleen extended downward to the floor of the pelvis. The entire operation lasted less than one-half hour. The condition immediately after operation was good. The blood examination after operation was: red blood-cells, 3,860,000; leukocytes, 19,600; hemoglobin, 66 per cent.; differential count—polynuclears, 72 per cent.; large lymphocytes, 20 per cent.; small lymphocytes, 8 per cent.

Within a few hours the temperature rose to 104 F., and the child died the following day.

The spleen immediately after operation weighed 490 gm. and measured 18 by 9.5 by 5 cm. The general configuration was quite normal, though the organ was slightly elongated. The surface was smooth; the color a peculiar brownish-salmon; on section, the surface was mottled, due to the presence of transparent pearly areas, mixed with minute hemorrhagic spots. There were no tubercles present, no large nodules nor areas of necrosis, the entire surface presenting a mottled homogeneous appearance.

The necropsy was performed in my presence by Dr. Thalheimer. The heart, lungs, larynx, trachea and bronchi were normal; the tracheobronchial nodes were enlarged; thymus and thyroid were normal; there was no free fluid in the abdomen; no oozing from the stump. The liver weighed 730 gm.; the size was 20 by 13 by 6.5 cm. It extended 6 cm. below the free border of the ribs. The surface was smooth and glistening and the color was light pinkish-yellow, the capsule was not thickened; on section the same color was seen. The lobules were but poorly outlined and some diffuse gray areas were noted. A few white irregularly shaped areas were present, varying in size from 2 mm. to 1 by 1.5 cm. in diameter. They were situated around the medium-sized blood-vessels and slightly raised above the surface. Their borders were not well defined and the outlines of the lobules could barely be determined in them. At the hilus were about twelve enlarged lymph-nodes from 1 to 2 cm. in diameter; these were very friable, semitranslucent and of light brownish-gray color; on section the same color was seen and they were quite succulent in character.

The kidneys, adrenals, esophagus, stomach and intestines were normal. The abdominal lymph-nodes were enormously enlarged, many of these being from 1 to 2 cm. in diameter. The pancreas was normal; the bone-marrow was of bright red color, with small white dots.

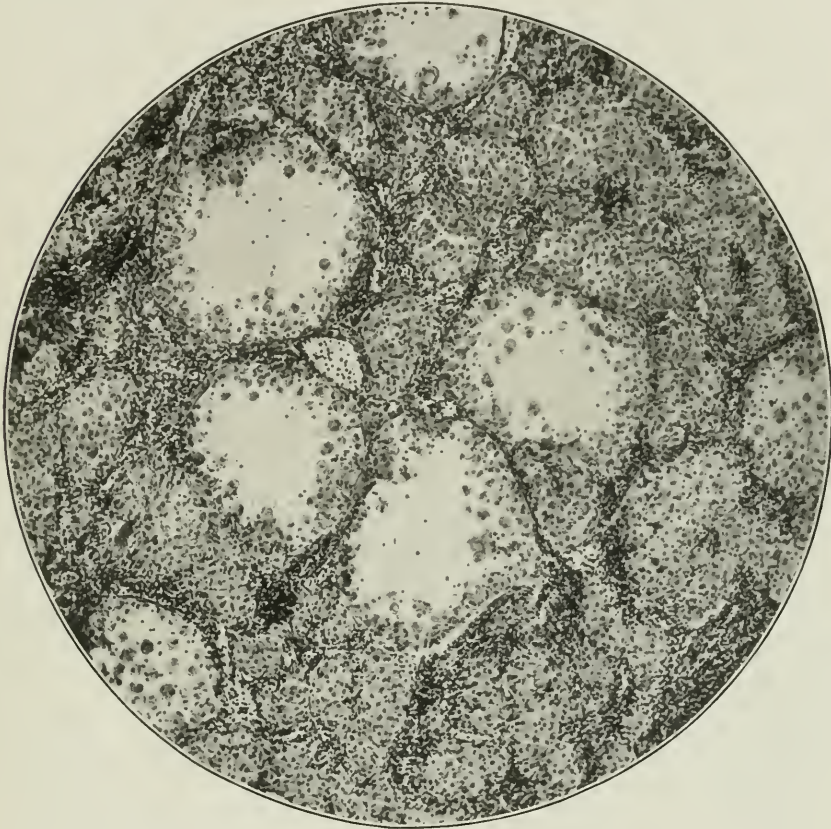
The microscopic examination of the organs was carried out by Mandelbaum² and I am indebted to him for the opportunity of studying many of the slides with him.

Smears were made from a freshly cut surface of the spleen shortly after its removal. The cells presented the general appearance described by all previous observers; study of sections of the spleen with low power revealed many large round or oval spaces, with well-defined outlines; these were the venous sinuses. The sections also contain a large number of similar alveolar spaces, filled with large cells; the large cells are identical with those found in all the previous cases; isolated groups of large cells were seen between the lymphoid cells of the follicles, often near the peripheral part. Throughout the sections were mononuclear cells, with eosinophil granulations; within the lumen of the venous sinuses, no reticulum fibers were seen; there were no areas of degeneration, necrosis or hemorrhage in the spleen, and no evidences of a tuberculous process (see illustration).

2. Mandelbaum: *Jour. Exper. Med.*, 1912, xvi, 6.

The degree of involvement of the lymph-nodes varied considerably in the different groups of nodes, but the type of lesion corresponded with that described in other cases; the retroperitoneal and the mesenteric nodes showed the greatest involvement; the pigment in these nodes is quite abundant; it is never free but is always situated in cells of various sizes.

The large endothelial cells were very numerous in the bone-marrow. Sections from some portions of the liver were quite normal, while other parts showed the characteristic lesion.



Splenomegaly Gaucher type; $\times 80$

Mandelbaum summarizes the pathologic findings in this case as follows: "The lesions are found in the spleen, lymph-nodes, bone-marrow and liver. These organs show the presence of iron-containing pigment, and large multinuclear cells with a characteristic cytoplasm. In the early cases peculiar large phagocytic cells arising from atypical large lymphocytes are found in the follicles (*Keimcentra*) of the hemopoietic system. After leaving the follicles these cells possess phagocytic qualities for a certain period. As a result of the phagocytosis the cells enlarge, the nature of the cytoplasm changes, and the cells acquire a characteristic vacuolated and wrinkled appearance. The cells are carried from the spleen through the portal system to the liver, where they are destroyed. The irritation produced by this destructive process gives rise to an increase in the intralobular connective tissue."

EPITOME OF ALL THE CASES OF SPLENOMEGALY GAUCHER (IN CHILDREN)
REPORTED IN THE LITERATURE

COLLIER'S CASE 1.³—The spleen was taken from the body of a female child aged 6 years, who was admitted to Radcliffe Infirmary April 4, 1894, and died there Sept. 7, 1894. The mother stated that the child was healthy up to 8 months, when she had a severe illness the nature of which is not known. When

FINDINGS IN THE CASES—

	Case No.	Sex	Age	First Splenic Enlargement Noted at Age of	Spleen Enlarged	Liver Enlarged	Hemoglobin	Red Blood-Cells	White Blood-Cells
Collier	1	♀	6	2	+	+	†	†	†
	2	♀	10	?	+	+	?	?	?
Bovaird	3	♀	6	3	+	+	60	2,880,000	4,000
	4	♀	13	3	+	+	75	4,440,000	9,000
De Jong and Van Heukelom.....	5	♀	12½	7½	+	—	65	4,782,000	3,800
	6	♀	18	8	+	+	90	4,136,000	3,100
	7	♂	15	?	+	+	70	3,908,000	3,700
Reuben	8	♀	8	4	+	+	68	3,440,000	6,200
	9	♂	4	4	+	+	35	2,208,000	5,000
Niemann	10	♀	17 *	2 *	+	+	‡	‡	‡
Erdmann and Moorhead.....	11	♂	8½	1¼	+	+	62	3,912,000	4,600
	12	♀	3½	1¼	+	+	56	5,000,000	9,800
Bernstein	13	♀	7	6	+	+	?	?	?
	14	♂	14½	6½	+	+	30	2,560,000	2,400

♂—Denotes male. ♀—Denotes female. * Months. † R. B. C. misshapen; no excess

‡ Since my article was submitted for publication, Dr. J. H. Mason Knox, Jr., and Dr. (abstr. *Arch. Pediat.*, June, 1914, p. 467). The patient was 11 months old, had never lymph glands and a peculiar yellowish pigmentation of the skin of the exposed parts, ance characteristic of lymphatic leukemia. The picture in the spleen resembled that first and until the full report of the case is published it is best not to include it among the

2 years old the abdomen was noticed to be enlarged, and was steadily increasing in size. The blood was examined, but no excess of white blood-corpuscles was found. The red blood-corpuscles were misshapen and did not form good

3. Collier: A Case of Enlarged Spleen in a Child Aged 6, *Tr. London Path. Soc.*, 1895.

rouleaux. Slight bending of ribs, but no other signs of rickets, was present. Death seemed to be accelerated by an attack of "epistaxis and sickness." The mother stated that she had seven children, four of whom died previously to this one—one of inflammation of the lungs, two of consumption of the bowel and one in the infirmary six years previously.

Necropsy showed no tuberculosis; spleen weighed 4 pounds 2 ounces; child 23 pounds; all mesenteric glands enlarged.

—IN THE LITERATURE†

Pigmentation	Location of Pigmentation	Hemorrhages	Splenectomy	Necropsy	Survived Splenectomy	Cause of Death	Wt. of Spleen, gm.	Weight of Liver, gm.
?	?	Epistaxis	..	+	..	Disease	2,070	
?	?	?	..	+	..	Disease	875	
Bronzed	Face, nose, hands	Epistaxis						
Bronzed	Face, nose	?	+	+	..	Splenectomy	6,200	2,380
Yellow brown	Abdomen	Oozing gums	+	..	+	1,850	
Brown	Abdomen	Menorrhagia						
No pigmentation	..	Epistaxis						
Roman gold	Face	?						
Roman gold	Face, Hands	Epistaxis	+	+	..	Splenectomy	490	730
Pale brown	Face	?	..	+				
Looked dark	?	Epistaxis	Disease		
?	?	?	+	..	+	430	
?	?	?						
Dark brown	Face	Epistaxis hematemesis	+	..	+		1,320	

of W. B. C. ‡ Normal in every respect.

R. H. Wahl reported a case of this disease (?) before the American Pediatric Society thrived and weighed 11 pounds. There was idiopathic enlargement of the spleen, liver, The blood-picture was normal until a few days before death, when it assumed the appearance described by Gaucher in 1882. From the abstract quoted it is hard to classify this case authentic cases.

COLLIER'S CASE 2.—The sister died at an infirmary Nov. 27, 1888; was admitted with bronchitis and enlarged spleen; gradually lost strength and died of exhaustion. No tuberculosis was found on necropsy. The spleen was found to be enormously and uniformly enlarged; weight 25 ounces. On section it was found congested and its substance was firm though somewhat friable. (Reported Jan. 16, 1895.)

BOVAIRD'S CASE 1.⁴—Female, aged 3; father and mother living and well; nine children; one stillbirth at eight months; four died during infancy from summer complaint; five are living; no previous diseases.

For about one year the mother noted enlargement of abdomen, steadily increasing; also noted a mass on right side of abdomen as well as on left; was sent to hospital; the child was of normal stature, well nourished, not anemic; skin dusky; some signs in the lungs; liver dulness from fourth space to 3 inches below free edge of ribs; edge was hard and sharp; spleen extended to within $\frac{1}{2}$ inch of median line at umbilicus; lower end on a level with anterior superior spines of ilium; edge sharp and hard; nodes in each axilla; one node the size of a bean; both sets of inguinal glands were slightly enlarged, not tender, freely movable. Blood, 4,400,000 reds, 9,000 whites, hemoglobin 75 per cent.

The child was in the hospital from Nov. 28, 1896, to Dec. 22, 1896; seemed quite well; chest signs cleared up; gained $1\frac{3}{4}$ pounds. Treatment, Fowler's solution.

Some time prior to July 26, 1899, the child had been failing; nose bled frequently and quite severely; lost flesh; face and hands had become bronzed. At this time—age 6 years—across the bridge of the nose and on the cheeks and hands there was diffuse bronzing of the skin; abdomen spare, prominent; superficial veins enlarged; liver extended from sixth rib to within $1\frac{1}{2}$ inches of umbilical line. The spleen later extended into and filled the right iliac fossa. The glands, inguinal, cervical and axillary, were slightly enlarged. Blood, 4,180,000 reds, 14,000 whites, hemoglobin 62 per cent. In December, 1899, the child had not improved but was able to attend school.

BOVAIRD'S CASE 2.—Female, sister of above patient, aged 13, had measles at 5 years; at 7 an eruption on the scalp. At the age of 3 the mother noticed an enlargement of the abdomen which progressively increased in size, and also pigmentation of the skin, especially across the nose. The child complained of a little discomfort from the enlarged abdomen and was a little short of breath. When admitted to the hospital she was small in stature for her years, fairly well nourished, skin dusky; across the nose, underneath the eyes and on the upper lip there was a decided brownish pigment. Liver dulness extended from the fifth space to the margin of the ribs; edge could not be felt; superficial veins were dilated. The spleen extended to 1 inch above the umbilicus, passed obliquely to the anterior superior spines and was hard and smooth. There was slight enlargement of right inguinal nodes, moderate enlargement of both submaxillary and one palpable node in each axilla; no enlargement of the epitrochlear nodes. Blood, 2,880,000, reds, 4,000 whites, hemoglobin 60 per cent. Mixed treatment was tried without effect. Three years later the condition was the same; the child did not grow in stature or gain weight. Readmitted to the hospital in 1899, aged 16 years. The patient was fairly well nourished, face and hands deeply bronzed; liver dulness began at the sixth rib; edge $1\frac{1}{2}$ inches below the free costal margin; the spleen filled the whole of the left iliac fossa. Blood, 3,550,000 reds, 7,000 whites, hemoglobin not stated. Splenectomy was performed May 17, 1899, by Dr. A. J. McCosh. The patient died three hours after operation. The spleen weighed $12\frac{1}{2}$ pounds.

DE JOSSELIN DE JONG AND VAN HEUKELOM'S CASES.⁵—Father, a Jewish merchant 54 years old, has tabes; mother 50 years old and is healthy. The oldest of eleven children is 28 years old, the youngest 10 years old. Only six of

4. Bovaird: Primary Splenomegaly—Endothelial Hyperplasia of the Spleen—Two Cases in Children; Autopsy and Morphological Examination in One, *Am. Jour. Med. Sc.*, 1900.

5. De Josselin de Jong, R., and van Heukelom, J. Siegenbeck: Beiträge zur Kenntnis der grosszelligen Splenomegalie (Typus Gaucher), *Beitr. z. path. Anat. (Zeigler)*, 1910, xlviii, 598.

these could be examined; of these three had enlarged spleens and livers (the seventh, eighth and tenth were affected); no children died and there were two miscarriages.

CASE 1.—Betsy, 12½ years old; first observed at age of 5½ years; at 7½ years was brought to hospital for enlargement of abdomen. The child complained of weight in lower abdomen; was easily tired and complained of pain in left side; splenic and hepatic enlargement was noted at this time. At 10 years abdomen is still larger; child complains of morning nausea and occasionally vomits. In the last few years oozing from gums has occurred. Child never had any fever; only had measles previously. Skin of face is white and pale; the cheeks red; the skin of the body, especially the abdomen is of a light yellow brownish hue; veins of abdomen dilated; blue spots (mongol spots) on abdomen and back. Lymph-glands are not enlarged; no bone tenderness, no ascites; the liver two finger-breadths below the free border of the ribs; the spleen reaches to symphysis and is very hard; no urobilinuria. Blood examination: hemoglobin, 65 per cent.; red blood-cells, 4,782,000; white blood-cells, 3,800 (from 2,200 to 3,800); polynuclears, 51 per cent.; mononuclears, 46.5 per cent.; eosinophils, 2 per cent.; basophils, 0.5 per cent.; 1 myelocyte and 1 normoblast; von Pirquet negative; Wassermann negative. On Roentgen-ray and arsenic treatment the patient became worse and the hemoglobin came down to 55 per cent. The diagnosis of splenomegaly Gaucher was made, and the child was referred to Dr. Van Rossen for splenectomy. One day after operation the hemoglobin was 65 per cent.; red blood-cells, 4,960,000; white blood-cells, 15,500; the general condition became much better; the oozing from the gums stopped; the tiredness and nausea disappeared. Six months later the child's condition was excellent; the liver, however, had grown larger and was now palpable four finger-breadths below the free border of the ribs. The blood examination at this time showed: hemoglobin from 80 to 85 per cent.; red blood-cells, 4,920,000; white blood-cells, 14,400; polymorphonuclears, 54 per cent.; eosinophils, 10 per cent.; small lymphocytes, 18.6 per cent.; large lymphocytes, 10.6 per cent.; transitionals, 6.8 per cent.

CASE 2.—Sara T., aged 19, first observed at age of 13 years, at which time a hepatic and splenic enlargement was found. Blood: hemoglobin, 79 per cent.; red blood-cells, 3,500,000; white blood-cells, 4,350. First enlargement of abdomen noted by mother when child was 8 years old. At 17 child complained of pain in side and had a feeling of weight; at times complained of nausea; no oozing from gums; no epistaxis. Skin is white with the exception of a few yellow brownish stains on abdomen; no enlarged veins of abdomen; no ascites; no bone tenderness. The liver is hard and is especially enlarged in the horizontal direction; the spleen is hard and passes the median line. The hemoglobin is 90 per cent.; red blood-cells, 4,136,000; white blood-cells, 3,100.

CASE 3.—Brama de J., 15-year-old boy; never complained of anything. On examination spleen and liver were found to be enlarged. Boy had frequent epistaxis; no oozing from the gums; skin of normal color; glands normal; abdomen enlarged. The liver is three finger-breadths below free borders of ribs; the spleen is enlarged to the navel; no ascites. Blood examination: hemoglobin, 70 per cent.; red blood-cells, 3,968,000; white blood-cells, 3,700; polynuclears, 64 per cent.; eosinophils, 3.3 per cent.; small lymphocytes, 19 per cent.; large lymphocytes, 7.3 per cent.; transitionals, 6.3 per cent.; von Pirquet negative.

NIEMANN'S CASE.⁶—Irene D., 17 months old; sick since age of 2 months at which time the spleen was enlarged; from birth was a difficult feeding case. The emaciation was progressive; the abdomen was progressively growing

6. Niemann, Albert: Ein unbekanntes Krankheitsbild, *Jahrb. f. Kinder.*, January, 1914.

larger. At time of admission to the hospital, the infant was apathetic, very much emaciated and backward in its physical development. The abdomen was very large. The face had a striking pale brown discoloration; there were a few mongol spots on the dorsum. The eyes were slanting and the facies were mongoloid. The abdomen measured 50 cm. The liver and the spleen were both enlarged; the spleen reached below the navel; the lower edge of the liver could be felt over the anterior-superior spine of the iliac crest. The abdominal veins were widely dilated. A small amount of free fluid could be demonstrated in the abdomen; there was slight edema of the feet, and other signs of venous obstruction were present. The blood was normal in every respect. There was no icterus. The stools were normal. The Wassermann reaction was strongly positive (?); a rigid mercurial treatment was absolutely ineffectual. The infant's condition became steadily worse; the symptoms of venous stasis became aggravated, and the infant died of exhaustion four weeks later. For a few days before death the patient had irregular temperatures up to 39° C. At necropsy no luetic changes were found in any of the organs. The spleen, the liver and the abdominal lymph-glands showed the same kind of cells found in the other authentic cases of splenomegaly Gaucher. Although the writer reports the case as one presenting "an unrecognized disease picture," one glance at the photomicrograph which is included in his article leaves no doubt that his was a true case of splenomegaly Gaucher.

ERDMANN AND MOORHEAD'S⁷ CASE 1.—Parents are robust; no constitutional diseases. Henry, born March 1, 1901; breast-fed; weight at 1 year 18 pounds 4 ounces; abdominal protrusion first noted July 2, 1902; splenic and hepatic enlargement were noted at this time by Dr. W. C. Walsen; blood showed malarial parasites. The infant improved with treatment. January, 1903, the blood showed hemoglobin, 62 per cent.; red blood-cells, 3,912,000; white blood-cells, 4,600; small mononuclears, 12.5 per cent.; large mononuclears, 20 per cent.; polynuclears, 50 per cent.; basophils, 6 per cent.; eosinophils, 12.5 per cent. One month later child had colitis. September, 1906, blood was the same as in January, 1903; diagnosis of splenic anemia was made. January, 1907, the child had pneumonia; cough lasted all spring. The child died of pneumonia Oct. 27, 1909, after one day's illness; no necropsy. "At no time were any hemorrhages, except slight epistaxis. On one occasion, in the latter months, he vomited a great deal and often looked dark and blackened."

Second and third children were perfectly well and showed no splenic nor hepatic enlargement.

ERDMANN AND MOORHEAD'S CASE 2.—Fourth child, Elizabeth, was born Feb. 19, 1909; was breast-fed until 7 months; weight 14 pounds 10 ounces. Nov. 27, 1910, child had bronchitis, sick 10 days. At 1 year weighed 18 pounds. April 8, 1910, spleen was found slightly enlarged. Blood at this time: hemoglobin, 70 per cent.; red blood-cells, 2,956,000; white blood-cells, 14,000; small mononuclears, 13 per cent.; large mononuclears, 28.6 per cent.; polynuclears, 41 per cent.; eosinophils, 2 per cent.; basophils, 2 per cent.; myelocytes, 12.3 per cent.; transitionals, 1 per cent. At this time she seemed "rather nervous and hard to nourish. The only illness was slight colds." May 27, 1911, considerable increase in size of spleen; liver normal. Sept. 23, 1911, the liver was found to be enlarged. Feb. 21, 1912, blood examination showed hemoglobin, 56 per cent.; red blood-cells, 5,000,000; white blood-cells, 9,800; polynuclears, 45 per cent.; lymphocytes, 55 per cent. The spleen reached up to the umbilicus; the liver was moderately enlarged; no ascites. The abdominal veins were enlarged. The inguinal glands were enlarged, all others were normal. The Wassermann reaction was negative. Feb. 28, 1912, hemoglobin was 85 per cent.; red blood-cells, 6,200,000; white blood-cells,

7. Erdmann, J. F., and Moorhead, J. J.: Splenectomy for Splenomegaly (Gaucher Type), *Am. Jour. Med. Sc.*, February, 1914.

7,000; small lymphocytes, 49.4 per cent.; large lymphocytes, 9.4 per cent.; polynuclears, 40 per cent.; eosinophils, 1 per cent.; basophils, 0.2 per cent.; no malarial parasites. March 2, 1912, the child was pale, poorly developed, somewhat dyspneic, abdomen protuberant, veins prominent, no ascites. The liver was 2 inches below the costal margin and extended well to the left. The spleen was firm, smooth, not tender and reached just below the umbilicus and well toward the median line. There was one enlarged lymph-node in the right inguinal region. There was no jaundice; no pigmentation. The sclerae were clear; the bones were normal. June 6, 1912, splenectomy was performed; histologic study of the spleen showed it to be a case of Gaucher's disease. "The striking lesion microscopically in the spleen is the presence of enormous numbers of large mononuclear cells. . . . The protoplasm is granular and stains faintly. A few of the cells contain vacuoles. Very rarely a cell with two or three nuclei is seen." Sections were also made by Mandelbaum, who found typical tubercles in addition. Nine days after the operation the blood was: hemoglobin, 85 per cent.; red blood-cells, 6,080,000; white blood-cells, 19,000; small lymphocytes, 24.4 per cent.; large lymphocytes, 20.4 per cent.; polynuclears, 52.6 per cent.; eosinophils, 2.2 per cent.; basophils, 0.4 per cent. September, 1912, child in good health; no dyspnea; no dilatation of surface veins; liver reaches about 1 inch below costal border; no inguinal adenitis. March 21, 1913, liver slightly larger than in September.

HERRMAN'S CASE.*—In March, 1912, Dr. Herrman presented before the pediatric section of the Academy of Medicine a case of splenic anemia in a boy of 12. Since then the boy had been subjected to a splenectomy and histologic examination of the spleen by Bernstein revealed that the patient was suffering from splenomegaly Gaucher. This boy had been under observation at the Vanderbilt Clinic since 1906, and among others I was firmly convinced that this was a true case of splenomegaly Gaucher long before the splenectomy was performed. The patient, Samuel N., was first observed in 1906 (7 years). Abdominal enlargement was first noticed at 4 years; abdominal pain for last six months; epistaxis three or four months ago. The blood showed: hemoglobin, 75 per cent.; red blood-cells, 4,390,000; white blood-cells, 4,000; polynuclears, 70 per cent.; lymphocytes, 29 per cent.; eosinophils, 1 per cent. Spleen extended beyond the median line and 3 inches below the level of the umbilicus. The liver extended 2 inches below the costal margin in the mammary line; no lymph-glands were distinctly enlarged. Blood examination in last five years: hemoglobin, 30 to 75 per cent.; red blood-cells, 2,560,000 to 4,600,000; white blood-cells, 2,400 to 6,800. In 1909 after extraction of a tooth there was oozing from the gums for some time, and one month later patient had abdominal pain and vomited a large amount of blood. There is no ascites. The Wassermann and von Pirquet tests are negative; there was bronzing of the skin of the face, the neck and the hands; a wedge-shaped conjunctival thickening on both sides, with the bases toward the cornea and the angles extending toward the nasal and temporal angles of the lids were present. The parents are healthy; eight other children all well; one died in infancy of convulsions. Since the patient was presented at the Academy of Medicine, splenic hepatic enlargement was observed in a sister of the patient.†

8. Herrman: Report of Meeting of Pediatric Section of Academy of Medicine, Arch. Ped., March, 1912.

† Since my article was submitted for publication there appeared a subsequent report of this case by Drs. Herrman, Roth and Bernstein. (A Case of Gaucher's Disease in a Boy Thirteen Years of Age. Splenectomy with Recovery, *Arch. Pediat.*, May, 1914. On Oct. 17, 1913, the patient was admitted to Lebanon Hospital. During the preceding two weeks he had had several severe hemorrhages from the nose and gums and was very pale. On one occasion he lost 6 ounces of blood. The patient complained of feeling badly, had lost weight

HISTORICAL

In 1882, in a thesis for his doctor's degree, Gaucher reported the first case of the disease which now bears his name. He considered the malady to be a primary epithelioma of the spleen.

In all there are sixteen authentic families reported in the literature, in which the diagnosis was definitely established; of these patients eight were children and nine were adults at time of report.

Various opinions have been expressed as to the nature of the disease; as yet there is very little agreement of opinion. It has been variously described as an endothelioma of the spleen, and as a "hyperplasia of the spleen characterized by an unusual development of endothelial cells, and the transformation of a considerable part of the organ into dense connective tissue." Others have thought that the large cells arose from endothelium or normal reticulum in the hemopoietic apparatus. Schlagenhauser considered the process to be a systemic disease of the lymphatic hemopoietic apparatus with proliferation of the reticular structures affecting the spleen primarily, then the regional and other lymph-nodes and finally, the liver and the bone-marrow. Von Herczel considered the spleen to be the seat of an inflammatory process or a new growth. It is evident that, while all are agreed as to the histological features of the lesion, the source and nature of the cells are still wrapped in mystery.

Various names have been suggested for this disease: "Gaucher's disease," "splenomegaly Gaucher," "large-cell glandular metamorphosis" (*grosszellige Drüsenmetamorphose*). As the hepatic enlargement in this disease is constant (in the advanced stages of the disease), and is of valuable diagnostic importance, and as its copresence with a large spleen is almost pathognomonic of this disease in children, I suggest the name of "splenohepatomegaly Gaucher" as one which gives a conception of the two most important symptoms of this disease and one which reflects credit on the discoverer of this ailment.

ETIOLOGY

Family Incidence.—The disease is undoubtedly congenital and usually affects more than one member in the same family; although it is familial it is not hereditary. In none of the cases here reported did the parents of any patient have this affection. Of the seven families here recorded there were three members affected in one family, two members each in five families, and one member in one

and was troubled with headache, dizziness, dyspnea and nausea. Splenectomy was performed on Oct. 22, 1913. The patient made a good recovery and was discharged Dec. 11, 1913. The spleen in this case measured 27 by 13 by 10 cm., and weighed 1,320 gm.

family. The total number of children born in these seven families was forty-four; of these, eight died during infancy of other ailments, fourteen had splenic and hepatic enlargement; the diagnosis was definitely established on necropsy or by examination of the spleen after splenectomy in eight cases.

Sex.—Of the eight patients in whom the diagnosis was definitely established, six were females and two were males; the case here reported being the first of a male child to be recorded. If we include the six other members of the families in whom the diagnosis was not definitely but presumably established, there were ten females affected and four males.

Age.—The youngest child reported was 17 months old. Arranged according to age at time of report, they were respectively: $3\frac{1}{2}$, 4, 6, 6, 8, $8\frac{1}{2}$, 10, 12, 13, $14\frac{1}{2}$, 15 and 17 years old. The earliest splenic enlargement was observed in one case at 2 months; in two cases at $1\frac{1}{4}$ years; in two cases at 3 years; in two cases at 4 years, at $6\frac{1}{2}$, $7\frac{1}{2}$ and at 8 years; so that on the average the first splenic enlargement was noted at $3\frac{3}{4}$ years.

PATHOLOGY

In five of the eight authentic cases, necropsies were performed, and in three the spleens were examined after operation. In the eight examinations of the spleens, the findings were almost identical in all the cases; Bovaird was first to note similar changes in the mesenteric glands, and Mandelbaum and Libman were the first to find the endothelial hyperplasia in the bronchial and retroperitoneal glands and in the bone-marrow.

Macroscopic Examination.—The liver is firm and smooth over the greater part, and is usually much enlarged; there is evidence of old and new infarcts; on section it is chocolate colored and there are numerous small white areas.

The spleen is much enlarged; the form of a normal spleen is retained; on the external surface fibrous adhesions are present; the surface is white to yellow, and in general is smooth; the fibrous coat is thickened; the substance is firm and resistant.

The appearance of the cut section varies; a central section shows firm yellow-white areas of pyramidal form; the remainder has the appearance of normal spleen.

Lymph-nodes are enlarged and soft; on cross-section the central parts are deep red and the periphery is pale.

Microscopic Examination.—Spleen: Sections from hard white areas differ from other sections that have the appearance of normal splenic tissue. In the latter sections there are large irregular spaces

filled with large, brightly stained cells. The walls of these spaces consist in part of a delicate line of connective tissue with infrequent small oval nuclei; adjoining spaces communicate with one another by narrow passages. The cells within the spaces are very large, and are of varied shape; many lie free in the spaces; these cells are round or oval. The nuclei vary considerably in size and shape; as a rule, they are very small in proportion to the size of the cell. There are also in some places giant cells. These spaces are the pulp spaces of the spleen, and the cells that fill them have sprung from their walls. The normal pulp cells have disappeared. On the other hand, the malpighian bodies are met with almost unchanged. The connective tissue in some places is so abundant that the spaces contain but one cell.

Sections from the white areas consist of dense connective tissue. In part this is infiltrated with small round cells; in other parts seems to be made up of a meshwork of capillaries.

Capsule and trabeculae are greatly thickened. The blood-vessels are surrounded by a greatly increased quantity of connective tissue.

The malpighian bodies "seem very little affected by the great changes that have gone on about them."

Liver: The capsule is thickened and the connective tissue throughout the organ is increased; the capillaries contain considerable pigment; the liver cells are normal; the bile ducts are normal; in the blood that fills the branches of the portal vein there are large cells of the type seen in the pulp spaces of the spleen. Endothelial cells are mostly seen in the interlobular connective tissue spaces; a few are seen in the lobule proper.

Lymph-Nodes: These are swollen, red and soft; each follicle is outlined by a wall of brightly shining, dark pigment. The part of the lymph-sinus not occupied by pigment is nearly completely filled with the above-described endothelial cells.

Bone-Marrow: Cells identical with those found in the above-described organs are also found in abundance in the bone-marrow.

SYMPTOMATOLOGY

1. *Enlargement of the Spleen.*—One of the first symptoms and signs noted by the parents and the patients is a mass in the left hypochondrium; this mass is not tender. There is a gradual but progressive enlargement of the spleen. The increase in size of the spleen in this disease is not surpassed by splenomyelogenous leukemia; it is surprising how large the spleen may become without causing any great inconvenience to the person, and the enlargement of the spleen takes place a long time before any secondary symptoms arise. In many cases the condition is discovered accidentally, when the patients apply

for treatment for other ailments. In almost all the cases the spleen passes the median line and the lower portion well fills the iliac cavity. The smallest spleen weighed 490 gm.; the largest spleen weighed 6,200 gm. The average of five spleens was 1,097 gm. The normal average weight of these five spleens should have been about 120 gm.; the spleens from the affected cases weighed from five to forty times as much as the normal spleens should have weighed. One obtains a better idea of how large the spleen may become in this disease, when we note that in Case 1 of Collier, the child weighed 23 pounds and the spleen weighed 4 pounds 2 ounces; and in Case 2 of Bovaird the child weighed 78 pounds and the spleen 12½ pounds. In health the relation of the spleen to body weight is as 1:400; in the last two cases, it was as 1:5 and 1:6.

Enlargement of the Liver.—In all the cases but one there was a concomitant enlargement of the liver; in Case 5 there was no vertical enlargement, but the liver was enlarged horizontally toward the left; however, after splenectomy the liver began to enlarge in the vertical direction also; this also occurred in Case 12. In two of the cases there was no hepatic enlargement when the spleen was definitely enlarged. It can be definitely stated that the splenic enlargement is primary and the hepatic secondary; sooner or later, however, hepatic enlargement takes place. In every authentic case of this disease, in the later stages, a hepatic enlargement could be demonstrated. In some cases, the liver increased in size proportionally to the spleen; in others it was slightly enlarged. In Case 10 the liver was larger than the spleen.

Enlargement of the Lymph-Nodes.—The lymph-nodes are usually normal. In Cases 3 and 4 there was slight enlargement, but I think we cannot positively rule out specific infection. There is a history of a stillbirth at 8 months, and four deaths in early infancy in that family. I am of the opinion that the glandular enlargement was probably due to an underlying luetic infection. Patient 12 had one enlarged inguinal gland; Patient 14 had palpable but not enlarged glands in the axilla and in the groins.

Blood-Changes.—The blood shows usually a mild anemia. The anemia varies from time to time and is subject to various grades of improvement; only in the later stages of the disease does it become progressive. In the stage at which there is no anemia, the red blood-cells may be up to 6,000,000. When anemia is present, they may be as low as 2,560,000. There is little, if any, change in the contour, shape or size of the red cells. The color may be paler than normal. In only two of the cases have nucleated forms been observed; in these a solitary normoblast was seen in each.

The white blood-cells are usually diminished in number, even when the red blood-cells are not. The lowest white blood-cell count was 2,500; the average white blood-cell count in nine cases was 5,160. A persistent leukopenia in the absence of anemia is a very suggestive symptom. Case 12 was the only one which at any time during the course of the disease had a leukocytosis, but even in this case there were periods of leukopenia. The hemoglobin varies with the anemia; usually there is greater reduction in the hemoglobin content than in the number of the red blood-cells, giving rise to a low color-index, and therefore of a mild anemia of the chlorotic type. It was as low as 30 per cent. in Case 14 and 35 per cent. in Case 9.

The differential count is usually normal; however, in Cases 5, 6 and 12 an eosinophilia of 10, 3.3 and 12.5 per cent., respectively, was found on various examinations. In all the cases reported, one or two myelocytes were found at every blood examination. In one examination in Case 12, 12.5 per cent. myelocytes were found. In all the cases in which there was leukopenia before operation, there was a leukocytosis of from 14,000 to 20,000 after splenectomy. Bone tenderness was not noted in any of the cases. Abdominal pain, especially over the splenic area, fulness and dragging sensation were noted in nearly all the cases.

The pigmentation has been variously described, varying from a brownish bronzing and Roman gold color, to a yellow, light yellow icteric hue. The pigmentation is seldom diffuse and usually affects the face, neck and extremities, the bridge of the nose, around the eyes and the cheeks being favorite spots. Pigmentation of the abdomen was observed in Cases 5 and 6. Mongol blue spots were observed in two cases. A brown-yellow wedge-shaped thickening of the conjunctivae of both eyes was observed in Case 14. This symptom is of some significance as it has also been observed in several authentic adult cases of this disease.

Hemorrhages as a rule are not severe, and are usually in the form of epistaxis or oozing from the gums. They are usually frequent; spongy gums were observed in five cases; menorrhagia and hematemesis were each observed once, in different cases.

Jaundice was not present in any one of the authentic cases; bile is not present in the urine and urobilinuria is not increased to any appreciable extent. The stools are normal and contain bile. Ascites is usually absent; in Case 10, slight ascites was present a few days before death. The superficial abdominal veins were dilated in a majority of the cases.

General Symptoms.—As the spleen and the liver become larger, the children begin to complain more and more of abdominal pain,

general discomfort, weariness and dyspnea. As the disease progresses and the anemia becomes more marked, emaciation becomes extreme. Patient 1 weighed 23 pounds at 6 years and Patient 4, 78 pounds at 16 years.

COURSE OF THE DISEASE

In infants and young children the disease is slowly progressive with a certain number of remissions. The younger the child is when the first splenic enlargement appears, the graver is the prognosis. This disease does not run so benign a course as it does in adults. Adults on the average live about nineteen years after they have contracted this disease and may live as long as thirty-six years after its inception. Adults afflicted with this disease usually die of some intercurrent affection. Infants and children, on the contrary, usually die of asthenia or rupture of the spleen brought about by the disease itself. In the fourteen cases, reports of which are here collected, seven patients died, five of the disease itself and two after splenectomy; Patient 4 being hopelessly moribund from the disease before operation. The prognosis in children is far graver than it is in the adult type of the disease, unless splenectomy is performed early. There are not sufficient data at hand to prove or disprove that splenectomy brings about a cure. Of the five cases in which splenectomy was performed, in two the patients died immediately after operation, and in the three patients who survived, the hepatic enlargement progressed after the splenectomy. Certainly splenectomy produces no such wonders in this disease as it does in Banti's disease and in splenic anemia. It relieves all the symptoms, but whether it produces a cure we have not sufficient data, pro or con. The three cases in which the patients survived splenectomy have not been observed sufficiently long to draw any definite conclusions from them. The pathologist must also tell us whether the lesion begins in the spleen and then spreads to the other blood-forming organs, or whether the power for the disease to progress lies latent in the other organs, and may become active even when the spleen is removed. Definite knowledge on this point is lacking. There is no agreement of opinion among the pathologists on this point. Some assert that the spleen is the primary seat of the disease and that the large cells in the course of the disease are transported to the other blood-making organs and there proliferate. In accordance with this view an early splenectomy should result in a cure. Others maintain that although the spleen is the first of the hemopoietic organs to show activity in this disease, the other blood-forming organs have the power latent in them from birth to become active and may cause enlargement of the liver, even after the spleen is removed. According to this view, splenectomy cannot stop the progress of the disease; it

can only relieve the symptoms due to the size and the weight of the spleen. In the progressive cases of infants and children, however, splenectomy is the only measure to be thought of for the temporary relief, if not for the cure of the disease, as the size of the spleen may be a direct menace to life on account of the danger of rupture. All other measures are futile.

DIAGNOSIS

This disease is not a manifestation of tuberculosis or syphilis. The Wassermann reaction was negative in Cases 5, 9, 12 and 14; it was positive in Case 10 (?), but on necropsy there was found not the slightest evidence of luetic infection.

In the stage of prehepatic enlargement, the following points are of diagnostic importance: the familial nature of the disease; persistent leukopenia, even in absence of anemia; progressive enlargement of the spleen in spite of the improvement of the anemia, if present, is almost pathognomonic; the conjunctival thickenings; the absence of all etiologic factors; the absence of jaundice, ascites, urobilinuria and fever, and splenic puncture. This procedure is hardly even used in the United States; in Italy, especially Florence, where it has been extensively tried, very few untoward complications have been observed from its use; as in very young children and in infants this disease is almost invariably fatal, a splenic puncture for diagnostic purposes should be performed in every case in which this disease is suspected; if examination of this material reveals it to be a case of Gaucher's disease, splenectomy should be urgently recommended, for it is these cases without hepatic enlargement that offer the best hope of permanent relief and cure of this disease.

In the stage in which both the spleen and the liver are enlarged, the diagnosis can more readily be made. There is no other disease of infancy and early childhood in which the liver and the spleen assume such enormous proportions; splenomyelogenous leukemia not excluded; this disease runs an afebrile course except in its terminal stage; here too the other symptoms are of great importance in arriving at a correct diagnosis; the familial predisposition; the persistent leukopenia; the conjunctival thickenings; absence of jaundice, ascites and urobilinuria; the presence of a brown yellow pigmentation, especially on the face, neck, extremities and the abdomen; the presence of oft-repeated but slight hemorrhages, mostly in form of epistaxis and oozing from the gums, which are usually spongy; the absence of all symptoms when anemia is not present, in spite of an immense liver and spleen; the progressive enlargement of the spleen and the liver, in the anemic stage, even when the anemia under treatment is rapidly disappearing; the absence of all glandular enlargement, and finally splenic or hepatic puncture.

DIFFERENTIAL DIAGNOSIS

The diseases from which it is especially to be differentiated are splenic anemia in adults and von Jaksch's disease in infants. Under the term "splenic anemia," Osler includes all those cases of idiopathic enlargement of the spleen associated with anemia, which were formerly classified as splenic pseudoleukemia, anemia splenica, lymph adénie splénique and splenic form of Hodgkin's disease. He states: "I purposely have not spoken of anemia with enlarged spleen in very young children, a subject which requires separate consideration."

The entity of splenic anemia is not at all granted. Stengel in his paper on "Splenic Anemia" says: "I have elsewhere expressed doubt regarding the individuality of such a condition and the conviction that many different sorts of diseases have been classed under this term."

The differential points will be noted from the following:

ANEMIA SPLENICA

Family Incidence: Not more than one in a family.

Sex: Males, 39 out of 47.

Age: Low limit (9-20) High limit (58-72).

Pathology: Spleen shows a hyperplastic fibrosis, involving particularly the malpighian bodies.

The liver shows no characteristic changes

The lymph-glands are not enlarged and show no changes.

The bone-marrow shows compensatory changes, secondary to secondary anemia.

Chronicity: Four to ten years.

Splenomegaly: Large.

Size of smallest spleen, 790 gm.

Size of largest spleen, 5,670 gm.

Average of fifteen cases, 1,883 gm.

Anemia: Secondary type.

Average red blood-count, 3,425,000

Average white blood-count, 3,850

Average Hgb. estimation, 47 per cent.

Hemorrhages: As a rule, hematemeses in one-half the cases; severe.

Ascites and edema: Occasionally seen.

Jaundice: Moderate in degree; veins in association with cirrhosis of the liver.

Liver: Is of normal size in most cases.

BANTI'S DISEASE

Sex: Female 32 out of 50 cases.

Heredity: Not congenital; does not affect more than one member of the same family.

Age: Youngest of 50 patients is 12 years; oldest of 50 patients is 55 years.

SPLENOMEGALY (GAUCHER)

Three families with two cases; two families with three cases.

Females: 12 out of 16.

Low limit (3-13) High limit (30-41).

Spleen, liver, lymph-glands and bone-marrow show endothelial hyperplasia.

Three to thirty-six years.

Larger.

Smallest, 430 gm.

Largest, 7,000 gm.

Average of nine cases, 4,300 gm.

Simple anemia.

Average, 4,000,000 reds; 5,600 whites;

Hgb. 70 per cent.

Rarely hematemeses, but epistaxis and oozing from the gums.

Never.

Never.

Greatly enlarged in a majority of the cases.

SPLENOMEGALY (GAUCHER)

Females 12 out of 16 cases.

Is probably congenital; usually affects more than one member of the same family.

Youngest recorded is 7 months; oldest recorded is 41 years.

BANTI'S DISEASE

Spleen much enlarged.
 Liver at first of normal size; then becomes enlarged, and later diminishes in size.
 Jaundice sometimes present.
 Ascites usually present.
 Blood: R. B. C., 4,330,000; W. B. C., 3,800; Hgb., 56 per cent.
 Hemorrhages: Usually severe, in the form of hematemesis.
 Duration seven to ten years.
 Death: Usually due to intoxication from cirrhosis of liver or to severe hemorrhage.
 Pathology: There is a fibrosis of the reticulum of the spleen, the liver and the portal vein. Bone-marrow and lymph-glands are normal.

SPLENOMEGALY (GAUCHER)

Larger.
 Always enlarged.
 Never present.
 Never present.
 R. B. C., 4,200,000; W. B. C., 6,000; Hgb., 70 per cent.
 Never severe; usually epistaxis or oozing from the gums.
 Three to thirty-six years.
 Usually due to intercurrent disease.
 There is an endothelial hyperplasia of the spleen, the liver, the lymph-glands and the bone-marrow.

In children it is most important to differentiate splenomegaly Gaucher from von Jaksch's disease (anemia pseudoleukemica, or according to more recent nomenclature, anemia splenica infantum). Differential points are as follows:

SPLENOMEGALY (GAUCHER)

1. Always primary.
 2. Usually affects children between the ages of 2 and 4 years.
 3. Discoloration usually yellow or orange; more marked in some parts.
 4. Spleen much larger; weighs 1,500 gm.
 5. Liver usually enlarged.
 6. Glands (lymph) never enlarged.
 7. Blood: Red blood-corpuscles, 4,100,000; white blood-corpuscles, 5,600; Hgb., 70 per cent.
- No abnormal cells found.

VON JAKSCH'S DISEASE

1. Usually secondary to gastro-intestinal disease, malnutrition, tuberculosis, lues, etc.
 2. Affects children between 6 months and 2 years.
 3. No discoloration, but there is extreme pallor of whole face, which may be olive color.
 4. Spleen enlarged but not to the same extent seen in S. (Gaucher). Spleen weighs 350 gm.
 5. Liver usually not enlarged.
 6. Lymph-glands sometimes enlarged.
 7. Blood: Red blood-corpuscles, 2,500,000 to 3,000,000; white blood-corpuscles, 10,000 to 20,000; Hgb., 45 per cent.
- Myelocytes and normoblasts up to 25 per cent in many of the cases.

In infancy syphilis and rickets are the most frequent causes of splenic enlargement; luetic splenomegaly is most common in the first three months of life and slightly declines as a cause of splenomegaly after this period, but even at from 9 to 12 months it is an important cause of such enlargement; rickets is the most frequent cause of splenic enlargement in infants after the ninth month; the absence of all other rachitic manifestations, makes differential diagnosis from this disease simple. Not one of the authentic cases showed any manifestations of lues, and in four out of five infants in whom the Wassermann reaction was tried, the reaction was negative.

There are several conditions which have a tendency to be familial and are associated with splenomegaly; the most important of these are: hypertrophic biliary cirrhosis (Hanot's cirrhosis), congenital hemolytic jaundice with splenomegaly, congenital obliteration of the bile ducts and Wilson's disease. Von Jaksch's disease, already differentiated, has been known to occur in three members of the same family, and in several instances in both of twins.

Hanot's cirrhosis is more common in males; the liver in this disease undergoes considerable uniform enlargement; the spleen is also enlarged and it may even become larger than the liver; there is jaundice, which becomes deeper during the "crises"; the urine contains bile; a moderate leukocytosis is present during the febrile periods, both of which are absent in Gaucher's disease; clubbing of fingers, deformities of the nails and other osteo-arthropathies have been described in children; the pigmentation is more extensive and the hemorrhages more severe than in splenomegaly Gaucher. This disease is sometimes encountered in several members of the same family, and it may be found in more than one generation of the same family; it is interesting to note that, in some members of these families, the spleen is enlarged though no symptoms are present.

In acholuric family jaundice, the jaundice appears at birth, or in later childhood; there is a general history of jaundice in other members of the same family; the urine is usually free from bile (acholuria); the condition is a chronic one and does not seriously endanger life except in early infancy; it is hereditary and has been traced for several generations in one family; both sexes appear equally affected; there is usually a slight enlargement of the liver and greater enlargement of the spleen; anemia may be severe and may prove fatal; normoblasts and megaloblasts are present. The jaundice may disappear to reappear at intervals in later life and thus obscure the diagnosis. The leukocytes are not affected in any characteristic way. There is an increased fragility of the red blood-cells, and there is a peculiar basophilic granulation of the red blood-cells on vital staining; on necropsy marked siderosis of all the viscera is found.

From congenital obliteration of the bile-ducts splenomegaly Gaucher is differentiated by the absence of a progressively increasing jaundice and severe hemorrhages and by its much more chronic course; the longest that infants have lived with this disease is ten months.

Kennier Wilson described a familial form of cirrhosis of the liver which is apt to occur in childhood; but the presence of mental symptoms easily differentiates this disease from splenomegaly Gaucher. In this disease various forms of disturbances of the central nervous system are present, giving rise to emotionalism, tremors, muscular rigidity.

contractions and mental symptoms. Signs of hepatic disease are usually absent during life; these cases are usually fatal; the average duration is 4 years.

In the anemic stage, Gaucher's disease is to be differentiated from the various forms of anemia and leukemia, splenic anemia, lues, tuberculosis, malaria, uncinariasis, kala-azar, malignant endocarditis, sepsis, new growths, primary and secondary, and mechanical obstruction to the portal circulation, as cirrhosis of the liver.

Examination of the blood will reveal the true nature of the blood diseases and of polycythemia with splenomegaly (*maladie de Vaquez*). Primary tuberculosis of the spleen is rare; there are usually other foci of tuberculosis present, polycythemia is often present in these cases, which is of diagnostic value; examination of the stool for ova will reveal the cause of the anemia if due to hookworm. Malaria can be easily ruled out on the absence of history of infection and on the examination of material from splenic puncture; the liver never assumes such large proportions in chronic malarial splenomegaly.

In the afebrile period of kala-azar differential diagnosis may be very difficult. The anemia is more severe in kala-azar and is usually progressive; the spleen and the liver are enlarged, but not to the extent that is seen in splenomegaly Gaucher. Sooner or later the fever returns; it is irregular and different in every case, and this irregularity is of very great diagnostic value. Hemorrhages are frequent and severe, and may have epistaxis, hematemesis, melena; the blood shows a leukopenia, with a relative lymphocytosis; positive diagnosis is made by the finding of the Pianese or of the Leishman-Donovan bodies in the blood, liver, spleen or bone-marrow. This disease runs a much shorter course (from five months to one year, subacute form; from two to three years, chronic form) and is almost invariably fatal.

Other diseases from which it is to be differentiated are, aleukemic leukemia, cirrhosis post leukemia, status thymicus, cirrhosis post myxedema, and the cirrhosis due to different causes as alcoholic, hematogenous, cardiac, metabolic, chromatic, adenomatosa and that due to tuberculosis, distoma and infections.

SUBACUTE ATROPHY OF THE LIVER

OCCURRING IN A CHILD FIVE MONTHS OF AGE *

ERNEST C. DICKSON, B.A., M.B.

SAN FRANCISCO

Subacute atrophy of the liver has been described by several authors during the past few years. It is a condition which closely resembles acute yellow atrophy of the liver in its etiology and initial symptoms, but it differs from acute yellow atrophy in that the progress of the disease is less acute, the onset of the second or terminal stage is delayed or absent, and fatal termination does not occur for weeks, months or even years after the initial symptoms. The condition is very rare. McDonald and Milne¹ collected the reports of the fifteen cases which had been reported previously to 1909, and added five new cases. Milne² has since reported one more case, and Fordyce³ had added another. In a fairly complete review of the literature I have been unable to find any other reported cases, although Milne mentions having seen specimens of four cases which have not been reported. In view of the infrequency of the condition it would seem justifiable to report the following case:

REPORT OF CASE

Baby C. was an apparently normal, 8-pound baby, the first child of young and healthy parents. He was breast-fed for about two months, after which he was placed on a formula diet. He thrived and steadily increased in weight. When about 2 weeks old he became deeply jaundiced, although there was no gastro-intestinal disturbance and no other sign of illness. The stools were not acholic. The child continued to grow and was apparently healthy, although the deep jaundice persisted. Dr. R. Langley Porter was called in consultation on account of the persisting jaundice when the child was about 3 months of age. He found a well-grown, well-nourished child which showed no abnormality except a marked jaundice, a palpable spleen and a slightly enlarged liver. The stools were not acholic and the child appeared healthy and happy. The blood of the child and of the parents gave a negative Wassermann reaction. Dr. Porter believed that the case was one of persistent icterus neonatorum. The child was seen only occasionally by the attending physician during the following weeks, but regular reports were received from the parents, who said that he was steadily gaining in weight although the jaundice persisted. Two months after Dr. Porter saw him, the child was seized with extreme respir-

*From the Division of Pathology of the Stanford University Medical School.

1. McDonald and Milne: Subacute Liver Atrophy, *Jour. Path. and Bact.*, 1908-09, xiii, 161. Contains a complete bibliography.

2. Milne, Lindsay S.: Subacute Liver Atrophy, *Arch. Int. Med.*, 1911, viii, 5, 639.

3. Fordyce, A. D.: Case of Subacute Liver Atrophy in a Child, *Proc. Roy. Soc. Med.*, 1910, iii, Part 1 (section for the diseases of children), p. 1.

atory distress, and there was marked abdominal distention which was thought to be due to intestinal gas. All efforts failed to relieve the condition of the patient, and Dr. Porter was again called in, but the child died before his arrival. Death occurred about twenty-four hours after the onset of the acute symptoms.

Partial necropsy was performed by Dr. Porter about twenty-four hours after death, and the organs were brought to the pathologic laboratory of the Stanford University Medical School for examination.

Necropsy Report.—The body was that of a well-grown, well-nourished male child of 5 months of age. There was marked jaundice of the skin and of the visible mucous membrane. There was a large hernia on the right side, which showed no evidence of strangulation. The abdomen was markedly distended and the flanks bulged prominently. The subcutaneous fatty tissue was well developed. The abdominal cavity contained about $3\frac{1}{2}$ pints of deeply bile-stained fluid, but the pericardium and the heart were apparently normal excepting for the marked icteric staining. The lungs were about normal in size, but showed some emphysema and some hyperemia and edema. There were a few hemorrhages beneath the visceral pleura. The peribronchial lymph-nodes were not enlarged. The spleen was large (9 by 7 by 5 cm.), smooth and firm. It was dark in color and the markings were not distinct.

The kidneys were very large (8 by 5 by 3.5 cm.), and showed the usual fetal lobulation. The capsules were not thickened and were not adherent. The surface of the kidney was mottled and opaque and showed several small hemorrhages. The cut surface was opaque and distinctly bile-stained. The bladder was filled with bile-stained urine. The adrenals were apparently normal.

The intestines contained fecal material which was well stained with bile.

The liver was very small (14 by 9 by 5 cm.), and was dark green in color. The capsule was not thickened, but the surface was everywhere finely granulated. The liver-tissue was very firm, and cut with considerable difficulty. It was everywhere dark green in color, and showed no definite lobular marking. Immediately beneath the surface was a narrow zone, about 3 mm. in thickness, in which there were many small nodules separated by narrow bands of denser, more grayish-colored tissue. In many places these nodules corresponded to the small irregularities on the surface of the liver. The gall-bladder was small but apparently normal, and contained bile. The larger bile-ducts were carefully dissected out, and showed no stenosis.

Microscopic examination of the liver showed complete absence of the normal liver structure. Around the periphery of the organ was a narrow zone of living tissue, the narrow, nodular zone described above, in which the nodules consisted of irregularly arranged accumulations of large cells, which were usually multinucleated, but which bore a close resemblance to liver-cells. The protoplasm of these cells stained clearly and showed but little evidence of fatty degeneration. The nuclei stained well, and where multiple, were often arranged around the periphery in such a way as to suggest a transverse section through an imperfectly formed tubule. In the center of these large cells was often an accumulation of bile pigment. A few of the cells in the nodules contained single, very large, deeply staining nuclei. There was no evidence of karyokinesis.

Between the nodules was a very cellular newly formed connective tissue interstitial substance, in which were many newly formed bile-ducts. For the most part these bile-ducts showed no communication with the interlobular bile-ducts or with the remnants of liver-cells, but here and there one was found which seemed to pass directly into one of the multinucleated structures. Scattered irregularly through the interstitial tissue were many isolated cells or bunches of cells which closely resembled liver-cells. Some of these cells contained but one nucleus, but many were multinucleated, and many contained bile pigment.

Beneath the narrow zone of living tissue was wide-spread necrosis which involved practically the whole of the liver, and in which all resemblance to normal liver structure was lost. The greater part consisted of fibrous tissue which contained practically no nuclei, and which stained very poorly with van Gieson's connective tissue stain. Scattered irregularly through this connective tissue were remnants of liver-cells which had completely lost their nuclear staining, and which contained many fat droplets and much bile pigment in their protoplasm. There was very little evidence of the interlobular bile-ducts, no new formation of bile-ducts, and no evidence of regeneration of liver-cells in this deeper necrotic portion, which formed by far the greater part of the total volume of the organ. There was no demonstrable lesion of the blood-vessels.

Sections of the kidneys showed marked destruction of the epithelium of the convoluted tubules, with complete necrosis in many places. The lumens of many of the tubules were completely blocked with desquamated epithelium and debris, and there was marked fatty degeneration of the still living epithelium. In places there was evidence of regeneration of the epithelial cells, but no karyokinesis was seen. Many of the smaller and collecting tubules contained bile-stained casts. The glomeruli showed practically no change. There was fairly wide-spread, somewhat patchy proliferation of the interstitial connective tissue which was quite cellular in type, and which contained many round cells. The blood-vessels were apparently normal.

Sections of the spleen showed marked passive congestion and beginning proliferation of the connective tissue of the pulp.

The pancreas and the thymus showed some irregular increase in the interstitial connective tissue, but the arteries were apparently normal.

The lungs showed some irregular areas of collapse, and moderate desquamation and fatty degeneration of the alveolar epithelium.

The adrenals showed no lesions excepting a few small hemorrhages into the medulla.

The diagnosis of the condition in this case presents considerable difficulty. At first sight the fibrosis in the liver, especially when associated with the beginning proliferation of connective tissue in the kidneys, pancreas and thymus, and with the medullary hemorrhages in the adrenals, suggests that the condition might be syphilitic. The complete absence of demonstrable lesion in the blood-vessels and the three negative Wassermann reactions, however, indicate that syphilis is probably not the etiologic factor in this instance.

The patency of the larger bile-ducts was easily demonstrated, and the presence of bile in the stools at all times precludes the possibility of the condition being due to a congenital stenosis of the biliary passage. Milne⁴ has reported a case of congenital stenosis of the bile-ducts in which the macroscopic appearance of the liver was apparently very similar to that in this case, but the microscopic picture was entirely different.

There seems little doubt that the case can best be described as one of subacute atrophy of the liver in which the onset was not accompanied by severe gastro-intestinal disturbances, and in which no

4. Milne, Lindsay S.: The Histology of Liver Tissue Regeneration, *Jour. Path. and Bact.*, 1908-09, xiii, 127.

definite etiological cause could be established. It is barely possible that there may have been an unrecognized infection of the cord which was responsible for the process, but certainly there was no reaction on the part of the patient which would suggest even a mild infection at the time of or preceding the appearance of the jaundice. In seven of the reported cases there was no recognizable etiologic factor, and they are described as being of insidious onset, and it seems justifiable to include this case in that group. The clinical history of the whole course of the disease is unfortunately not complete, but the examination made by Dr. Porter two months before the child's death showed that at that time, the liver and the spleen were larger than normal. This initial enlargement of the liver and the persisting enlargement of the spleen has been described in several of the reported cases.

The gross appearance of the liver differs somewhat from that of the majority of the reported cases in that the whole of the organ was stained dark green with bile. In the majority of the cases the livers were mottled in appearance owing to the presence of yellow nodules which were separated by a dark red "spleen-like" substance, but in one case described by Hlava,⁵ and in another described by Jores,⁶ portions of the liver were said to be dark green in color.

The gross appearance differs also in the regularity of size, and in the peculiar distribution of the nodules of regenerated liver-cells. In this case there is no evidence of a diffuse distribution of nodular hyperplasia, but practically all of the living tissue of the liver is found in a narrow zone, not more than 2 or 3 mm. in thickness, which lies immediately beneath the capsule. The distribution reminds one of the narrow layer of living tissue which is found immediately beneath the capsule in anemic necrotic infarction of the kidney. It is possible that the survival of this peripheral zone of tissue may depend on a partial blood-supply from the capsule, as is the case in the kidney, which enabled the peripheral cells to resist more effectively the toxic agent which caused the necrosis in the remaining portion of the liver.

The microscopic appearance of the living tissue corresponds closely to that described by the various authors with the exception that the nodules are all very small and are approximately of the same size. It is probable that the nodules represent areas of hyperplasia and proliferation of preexisting liver cells which survived the action of the toxic agent. The interstitial tissue, too, resembles that described by others. The newly formed bile-ducts are quite numerous, but for the most part could not be traced either to the preexisting interlobular bile-ducts, or to the cords or the remnants of cords of liver-cells.

5. Hlava, J.: Ein Fall von chronischer gelber Leberatrophie, *Prag. med. Wchnschr.*, 1882, vii, 303 and 313.

6. Jores: Zur Kenntniss der subakuten Leberatrophien, *Verhandl. d. deutsch. Path. Gesellsch. f. Chir.*, 1908, xi, 320.

In a very few places the new bile-ducts seem to pass directly into a multinucleated mass of protoplasm which resembles liver-cell protoplasm, and which apparently corresponds to the "knob" which was described by Klebs,⁷ and later by Meder⁸ and others, but the number of these "knobs" is so small that one would not be justified in attempting to determine their significance.

SUMMARY

The case is one of severe jaundice of obscure origin, occurring in a child 2 weeks of age, and persisting without intermission until the death of the child at 5 months of age. The child grew and developed in a normal manner, and was never acutely ill until within twenty-four hours of death. When the child was 3 months of age, the liver and the spleen were found to be enlarged, but no other abnormalities were found. The stools were not acholic at any time during the progress of the disease, and the Wassermann reaction was negative. Death was preceded by severe respiratory distress and there was marked abdominal distention. No history of convulsions was obtained.

Necropsy revealed a marked ascites, a small granular liver, a large indurated spleen, and large kidneys which showed marked parenchymatous degeneration. There was extreme general icterus, but no demonstrable stenosis of the bile-ducts.

Microscopic examination showed complete necrosis of the whole of the liver with the exception of a narrow zone around the margin where there was evidence of regeneration of liver tissue. The spleen, kidneys, pancreas and thymus showed some beginning fibrosis, but the blood-vessels in all the organs were apparently normal. There was marked parenchymatous and fatty degeneration and also necrosis of the renal epithelium.

The most interesting points in connection with the case are the following:

The obscure origin of the condition.

The remarkably little effect produced on the growth and development of the child.

The persistence of biliary secretion in the presence of extreme destruction of the liver tissue.

The persistence of life, and the absence of evidences of hepatic insufficiency when so small a portion of living liver tissue remained.

2294 Broderick Street.

7. Klebs (1868): Cited from Meder (see Note 8), and from McDonald and Milne (see Note 1).

8. Meder, E., Ueber acute Leberatrophie, mit besonderer berücksichtigung der dabei beobachteten Regenerationsercheinungen, Beitr. sur. path. Anat. u. zur. allg. Path., 1895, xvii, 143.

A STUDY OF TUBERCULOUS LESIONS IN INFANTS AND YOUNG CHILDREN, BASED ON POST-MORTEM EXAMINATIONS *

MARTHA WOLLSTEIN, M.D., AND FREDERICK H. BARTLETT, M.D.
NEW YORK

From July 1, 1908, until April 1, 1914, a period of almost six years, 1,320 autopsies were performed at the Babies' Hospital of the City of New York. Of these subjects 178 showed tuberculous lesions, or 13.5 per cent. of the total number, a proportion slightly lower than Lubarsch¹ found among 747 children up to the age of 5 years. Lubarsch's examinations extended over a period of five and one-half years, and he found 128 cases of tuberculosis, or 17 per cent. A study² of the earlier Babies' Hospital cases showed 16.4 per cent. tuberculous cases among 1,131 autopsies. The contrast with adult percentages is very striking, whether we accept Lubarsch's figures, 69.2 per cent., or those of Naegeli,³ 93.1 per cent. as the average.

In age the cases included in our study varied from 2½ months to 5 years, as follows:

2	were 2½ months old.
21	were from 3 to 6 months old.
23	were less than 6 months old.
50	were from 3 to 6 months old.
73	were less than 1 year old.
36	were from 12 to 18 months old.
25	were from 18 to 24 months old.
61	were from 1 to 2 years old.
134	were less than 2 years old.
28	were from 2 to 3 years old.
162	were less than 3 years old.
16	were from 3 to 5 years old.
178	

It will be seen that 75 per cent. of our subjects were under 2 years of age, and it is these young children who present the most interesting material for study. There was no instance of congenital tuberculosis in the series.

* From the Laboratory of the Babies' Hospital of New York City.

1. Lubarsch: *Virchow's Arch. f. path. Anat.*, 1913, cxxiii, 417.

2. Wollstein, M.: *The Distribution of Tuberculous Lesions in Infants and Young Children*, *Arch. Int. Med.*, 1909, iii, 221.

3. Naegeli, cited by Lubarsch (see Note 1).

This collection of cases divides itself into two main groups, according as to whether the lesions in the lungs and bronchial lymph-nodes were the predominating feature, or whether the lesions in the intestinal tract and mesenteric nodes were more marked. These two main groups may be subdivided as follows:

I. Pulmonary group:

1. Tuberculous lesions limited to the bronchial lymph-nodes.
2. Tuberculous lesions involving the bronchial lymph-nodes and one other organ:
 - (a) Lung.
 - (b) Pia mater.
 - (c) Fingers.
3. Tuberculous lesions involving the lungs and bronchial lymph-nodes as the most advanced lesion of a more or less generalized tuberculosis.

II. Intestinal group:

1. Tuberculous lesions limited to the mesenteric lymph-nodes.
2. Tuberculous lesions limited to the intestine and the mesenteric and cervical lymph-nodes.
3. Tuberculous lesions involving the intestines and mesenteric nodes as the most advanced lesion of a more or less generalized infection.

I. PULMONARY GROUP

It is rather interesting that not one of these young children came to autopsy with tuberculous lesions limited to the lungs, either in the acute or in the healing stage. The complete absence of such a case is evidence that the tendency of tuberculosis in young subjects is toward rapid generalization rather than toward localization and healing. Tuberculosis is a progressive and not a retrogressive process in infants; consequently tuberculous infection in early infancy leads to the death of the infant with comparative rapidity.

1. Tuberculous Lesions Limited to the Bronchial Lymph-Nodes

In five instances the tuberculous lesions were found to be limited to the bronchial lymph-nodes, only one node being involved in each of three cases, and two and three nodes in the other two cases respectively. These children were between 17 and 27 months old (two were 17, two were 18, one was 27 months); that is, they were not young infants—additional evidence that a localized or limited tuberculosis is very rare in early infancy, the tendency at that age being to rapid generalization of the infection. The lesion was an active one in every case, consisting of tubercles with cheesy degeneration of the greater portion of the nodes involved, accompanied in one instance by a small calcareous area within the cheesy mass. There was no evidence of encapsulation of the tuberculous lesion in any one of the affected glands. They were on the right side three times, on the left side once and at the bifurcation of the trachea once. The calcareous nodule was found in the oldest child of this group, a boy of 27 months, who had

undergone an operation for empyema four months before admission to the hospital, where he remained two weeks with unresolved pneumonia and an unhealed empyema. Two of the children died of lobar pneumonia, having given a positive von Pirquet skin test, which was explained at the autopsy by the tuberculous lymph-nodes. Another child died of embryoma of the kidney, and the cheesy lymph-node at the right lung root had not been suspected during life. The fifth case was that of a little girl who died of bronchopneumonia after acquiring esophageal stenosis by drinking strong lye solution. Tuberculosis had not been suspected in her case.

2 (a). *Tuberculous Lesions Limited to the Bronchial Nodes and Lung*

There were two children in whom the tuberculous lesions were limited to one lung and the adjacent bronchial lymph-nodes. One of these was a 4-months-old girl, the other a boy of 3 years. Both were admitted during the month of August for gastro-intestinal disturbance. Neither gave any family history of tuberculosis. In the older child a von Pirquet skin test gave a negative result, probably because the child was practically moribund at the time the test was made. At the autopsies the unsuspected tuberculous lesions were found, limited in the boy to a small area of cheesy pneumonia with beginning softening in the left lower lobe, and cheesy degeneration of several bronchial lymph-nodes on the left side. The younger child had two cheesy areas, 1 cm. in diameter, in the right apex, with a group of miliary tubercles in the adjacent lung substance and cheesy areas in most of the tracheobronchial lymph-nodes on the right side. These two cases demonstrate the lowered resistance of the young infant and of the older child with even a limited tuberculous lesion, to an attack of gastro-intestinal disturbance. The case of the younger child is also remarkable because of the limitation of tuberculous lesions to the respiratory tract in an infant of 4 months. The fatal intestinal attack evidently occurred before there had been time for generalization.

2 (b). *Tuberculous Lesions Limited to Bronchial Nodes and Pia Mater*

In the majority of cases, in our experience, tuberculous meningitis in young children is accompanied by tuberculosis of a number of other organs. An exception to this rule in the present series was that of a 27-months-old child who was admitted with the symptoms of tuberculous meningitis. Tubercle bacilli were found in the cerebrospinal fluid, and the von Pirquet test was positive. At the autopsy tubercles were found in the pia mater, and the only other tuberculosis in the body was that in two lymph-nodes at the bifurcation of the trachea. It is difficult to understand why other organs more sensitive to infec-

tion with the tubercle bacillus should have escaped being affected before the pia mater. It will also be noted that this child was in the third year.

2 (c). *Tuberculous Lesions Limited to the Bronchial Nodes and Fingers*

There was but one instance, that of a child 20 months old, who had but one other tuberculous focus besides that in the bronchial lymph-nodes. In this case several fingers were the seat of a dactylitis, apparently tuberculous. But since incision for closer examination was forbidden at the autopsy, positive proof of the nature of the process causing enlargement of the fingers is lacking. A positive von Pirquet skin test was obtained in this child during life.

3 (a). *Tuberculous Lesions of the Lungs and Bronchial Nodes as the Most Advanced Lesion in a Partially Generalized Infection*

As examples of pulmonary tuberculosis with beginning generalization through the blood-stream, we have an 18-months-old child in which there was tuberculosis of the lungs, bronchial lymph-nodes and spleen, and another in which tubercles were found in the liver, spleen and pia mater, in addition to the lungs.

The presence of recent tuberculous ulcers in the intestines in a boy 18 months old with an older infection in the lungs and bronchial glands suggested infection of the intestine through swallowing of tubercle-bacilli-laden sputum rather than blood generalization.

3 (b). *Tuberculous Lesions of the Lungs and Bronchial Nodes as the Oldest Lesion in a Generalized Infection*

By far the greater number of cases in this series fall into the group of primary pulmonary infection with markedly generalized tuberculosis by way of the blood. Thus, 134 of our 178 cases, or 75 per cent., were of this kind, the lesions in the lungs and bronchial lymph-nodes being older than those in any other organ involved. There were 72 cases with the most advanced focus in the right lung, 44 in the left lung, and 18 in which the lesions in both lungs were of equal age. In 40 cases the pulmonary lesion was one of miliary tubercles only, without any sign of cheesy degeneration. The lungs were free from tuberculosis in only 14 of the 178 cases.

Calcareous degeneration was found in the lungs only five times. Twice it was limited to one small nodule in the left apex, twice to the right apex, and in one instance two small calcareous areas, not more than 0.5 cm. in diameter, were present in the left upper lobe. Only two of these five children were less than 2 years old, the youngest 9 months and the oldest 27 months. In the lymph-nodes calcareous

degeneration of a tuberculous focus is rather more common than it is in the lungs, having been found in thirteen cases, in infants from 7 months to 3 years of age. Only two were under a year, four were between 1 and 2 years, and seven were over 2 years old. In twelve cases the bronchial lymph-nodes were the seat of a small calcareous lesion, in one a mesenteric lymph-node alone was affected, and in three cases both bronchial and mesenteric nodes were involved. In eight cases but one node was affected; in five instances from two to five nodes contained small calcareous areas. In no case, however, was the tuberculous lesion entirely calcified or encapsulated; that is, although an attempt to limit or heal the lesion was begun, it proved ineffectual in every instance. The absence of calcareous degeneration from tuberculous lesions of young infants is apparent; its rarity in children from 7 to 12 months is also plain, and finally its increasing frequency during the second and third years must be noted.

Pulmonary cavitation was present in forty-three children coming to autopsy, the location of the cavity varying as follows:

	Right	Left
In the upper lobe	16	14
In the lower lobe	11	6
In the middle lobe	4	0
	<hr/> 31	<hr/> 20

Six children had cavities in two lobes, one child had cavities in three lobes and three children had several small cavities in the same lobe. The cavities varied from 0.5 to 3.0 cm. in diameter, and were the result of softening of an area of cheesy degeneration. Many of them communicated with a bronchus, and the walls were always ragged, irregular, with blood-vessels sometimes present in them, or, rarely, crossing the cavity. The contents of the cavity were usually of a cheesy character, sometimes of grumous material. Pulmonary hemorrhages, probably because of the small size of the vessels present, did not occur in any of our cases. Twenty of the subjects with cavities were less than a year old, the youngest being $3\frac{3}{4}$ months, our observations thus confirming the well-known fact that cheesy degeneration in the lungs of these young children takes place and extends rapidly.

The more frequent involvement of the right lung is in keeping with the experience of other observers, and depends on the mechanical fact that the right main bronchus is shorter and straighter than the left.

II. INTESTINAL GROUP

1. *Tuberculous Lesion Limited to Mesenteric Lymph-Nodes*

But one child presented cheesy tubercles in one mesenteric lymph-node, without any other tuberculous focus in the body. He was 2

years and 10 months old, with no family history of tuberculosis, and entered the hospital for bronchopneumonia, of which he died. He had given a positive reaction to a von Pirquet skin test. That his tuberculous infection occurred through the digestive tract can scarcely be doubted. It must be noted that no case with tuberculosis of the intestines alone or of the intestines and mesenteric glands alone appeared in this series.

2. Tuberculous Lesions Limited to the Intestine and the Mesenteric and Cervical Nodes

In one infant, 9 months old, the mesenteric and cervical nodes were equally large and cheesy, while one deep cervical node contained a calcareous area; one tuberculous ulcer was found in the jejunum.

Whether the tubercle bacilli localized first in the intestines or in the lymph-nodes remains unsettled, and is rather immaterial—the point of the case being, that tuberculous infection followed deglutition, and not inhalation. In view of the calcification of the lesion in one cervical lymph-node, it would seem fair to assume that the lesion in this lymph-node was the oldest of the three.

3. Tuberculous Lesions of the Intestine and Mesenteric Nodes as the Oldest Lesion in a Generalized Tuberculosis

In two cases the cervical lymph-nodes showed as old a tuberculous focus as that found in the mesenteric nodes and intestines, while the liver and spleen and lungs contained but few young, miliary tubercles. The bacilli evidently were ingested in both these cases, and the cervical glands were infected at the same time as the mesenteric nodes.

Thirteen other cases presented the oldest lesion in the mesenteric lymph-nodes, whence more or less completely generalized infection had occurred. One child of 2 years, besides cheesy tubercles in several mesenteric glands, had miliary tubercles in the liver, peritoneum and pia mater. The involvement of the pia mater before that of the lungs and spleen is noteworthy. Six of the thirteen cases in which the mesenteric glands contained the oldest lesion were accompanied by tuberculous peritonitis. With one exception, a child of 7 months, all the cases of peritonitis occurred in children 21 months to 4 years of age.

Of the entire number of seventeen cases in which tuberculous infection resulted from deglutition and not from inhalation, six were less than a year old; two were 5 months old; one was 7 months; two were 9 months; 1 was 10 months; four were between 1 and 2 years; five were between 2 and 3 years; and two were over 3 years of age. The majority (65 per cent.) of these cases were beyond the nursing

stage, whereas in only 55 per cent. of the cases of respiratory infection were the children over 1 year old.

As for the dissemination of tuberculosis from a focus of ingestive origin, we find that in our series of seventeen cases the lungs were free five times, in three of which the bronchial-lymph-nodes were also free. In eleven children the lungs showed miliary tubercles only, never very numerous and always recent. In one case only were there conglomerate tubercles with areas of cheesy degeneration present in the lungs. This was in a child 21 months old, who showed the only very generalized tuberculosis among all the seventeen cases, ten organs being involved. The intestinal lesions were far older and more

TABLE 1.—

Case No.	Age, Yrs.	Bronchial Nodes	Lungs	Mes. Nodes	Intestines
1	5/12	0	Mil. tubercles	+	+
2	5/12	+	Mil. tubercles	++	+
3	7/12	+	Mil. tubercles	++	+
4	9/12	+	Very few recent tubercles	++	+
5	9/12	0	0	+	+
6	10/12	0	Very recent and few	++	++
7	1 5/12	+	Mil. tubercles	++	0
8	1 5/12	0	Mil. tubercles	+	0
9	1 6/12	0	Mil. tubercles	+	0
10	1 9/12	+	Mil. tubercles and cheesy areas	++	+
11	2	+	Mil. tubercles	++	++
12	2	0	0	++	+
13	2	+; 1 Cheesy	0	1 calcareous	0
14	2 10/12	0	0	1 cheesy	0
15	2 11/12	+; 1 calcareous	Mil. tubercles	++ Several calc.	+
16	3	0	Mil. tubercles	+	0
17	4	Early lesions only	0	+	+

extensive than were those of the lungs, and a very severe peritonitis was present.

A child 2 years and 11 months old showed a small calcareous area in one bronchial node, and several mesenterics had similar but larger areas. While the possibility of a simultaneous infection of both groups of lymph-nodes cannot be denied, the fact that there were only a small number of miliary tubercles in the lungs while tuberculous ulcers in the intestines were numerous, large and deep, points to the ingestive lesion as older than the inspiratory one.

Three of the children developed tuberculous meningitis, two having peritonitis as well, one with ten and one with five organs involved.

All the six infants under a year old had severe intestinal ulceration, while six of the older children showed no intestinal lesion. This was especially noteworthy in a child of 3 years with an extensive tuberculous peritonitis and caseation of many mesenteric lymph-nodes. Table 1 shows that marked generalization is not the rule in cases of tuberculosis of ingestive origin.

In two cases infection was traced to a circumcision wound, once in a young infant of 3 months⁴ and again in an older boy of 3 years. In both of these cases the oldest tuberculous lesion was in the inguinal glands and all the abdominal viscera as well as the retroperitoneal glands were affected.

—DEGLUTITION CASES

Cervical Nodes	Peritoneum	Liver	Spleen	Kidney	Pia Mater
+	0	+	+	0	0
0	0	+	+	+	0
0	+	+	+	0	0
0	0	+	+	0	0
+	0	0	0	0	0
0	0	+	+	0	0
0	0	+	0	0	0
+	0	+	+	+	0
+	+	+	+	+	+
0	+	+	+	0	0
0	+	+	0	0	+
0	0	+	+	0	+
0	0	0	+	0	0
0	0	+	+	+	0
0	+	+	+	0	0
0	+	+	+	0	0

Finally there were thirteen cases in which, at autopsy, the point of entrance of the tubercle bacillus could not be determined with certainty, because pulmonary, intestinal and glandular lesions were equally extensive and advanced.

CASES WITHOUT LUNG INVOLVEMENT

There were only fourteen cases in which the lungs were not involved. Of these, two children were less than a year old (the youngest being 8 months); five were between the ages of 1 and 2 years; seven were over 2 years old.

4. Holt, L. E.: Arch. Pediat., 1913, xxx, 696.

These 14 cases include 5 in which the bronchial lymph-nodes alone were affected; 1 with lesions of the bronchial lymph-nodes and pia mater; 1 with lesions of the bronchial lymph-nodes and fingers; 1 in which the mesenteric glands alone were involved; 2 in which the tuberculous lesions were limited to the bronchial glands, liver, spleen and pia mater; 1 in which the mesenteric glands, peritoneum, liver and pia mater were affected; 1 involving the mesenteric glands, intestines, spleen and cervical glands; 1 involving the mesenteric glands, liver, spleen, kidneys, bronchial glands and pia mater; and 1 with lesions in the mesenteric glands, liver, spleen, intestines, peritoneum and bronchial glands. Table 2 shows these cases at a glance.

TABLE 2.—CASES WITHOUT—

Case No.	Age, Yrs.	Bronchial Nodes	Mesenteric Nodes	Cervical Nodes
1	8/12	Right cheesy; one calcareous area	0	0
2	9/12	0	+	+
3	1 5/12	One on right side cheesy	0	0
4	1 5/12	One on right side cheesy	0	0
5	1 6/12	One on right and one at bifurcation cheesy	0	0
6	1 6/12	One on right and one on left cheesy	0	0
7	1 8/12	One on right side cheesy	0	0
8	2	One on left side cheesy	1 calcareous	0
9	2	0	+	0
10	2 3/12	Two at bifurcation cheesy	0	0
11	2 3/12	One on right calcareous	0	0
12	2 10/12	0	1 cheesy	0
13	4	One on right side cheesy	0	0
14	4	Only early tubercles	+	0

Of these fourteen cases nine were due to infection by inhalation and five to infection by deglutition. Seven of the former were cases in which the lesions were limited to the bronchial glands (or with the pia mater and fingers). Of the other five deglutition cases, in which the primary lesions were found, either in the mesenteric glands or in the intestines, with or without tuberculous peritonitis, one child was 9 months old and the other four were over 2 years. In the respiratory cases the children were somewhat younger, one being 8 months old, five between 1 and 2 years, and three over 2 years.

CASES WITHOUT INVOLVEMENT OF BRONCHIAL LYMPH-NODES

In the entire series of 178 cases there were only nine in which the bronchial lymph-nodes contained no evidence of tuberculosis. In

three the lungs were also free. In the remaining six there were tuberculous lesions in the lungs, but the primary focus was in the gastrointestinal tract. The youngest of these children was $5\frac{3}{4}$ months old; the oldest, 3 years.

THE MESENTERIC LYMPH-NODES

The mesenteric lymph-nodes, on the other hand, were the seat of a tuberculous lesion in 113 of the 178 cases. They showed a lesion less advanced than that in the bronchial lymph-nodes in 84 instances, in the same stage of development in 12, and older than the bronchial gland lesion in 17, in 9 of which the bronchial glands were not

—INVOLVEMENT OF THE LUNGS

Intestines	Liver	Spleen	Kidneys	Peritoneum	Pia Mater
0	+	+	0	0	+
+	0	+	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	+	+	+	0	0 Fingers +
0	+	0	0	+	+
0	0	0	0	0	+
0	0	0	0	0	0
0	0	0	0	0	0
0	+	+	0	0	+
+	+	+	0	+	0

involved at all, while the mesenteric nodes contained cheesy tubercles. There were only 4 instances of calcareous areas in mesenteric nodes, compared with 12 in bronchial nodes. In only 17 of these 178 cases were the mesenteric gland lesions the most advanced in the body, and in 4 of the 17 the intestines were not involved. The greater frequency of bronchial than of mesenteric gland involvement is apparent.

INVOLVEMENT OF THE MENINGES

Tuberculous meningitis occurred in sixty-nine, or 38 per cent., of these children. The youngest child with tubercles in the pia mater was $2\frac{1}{2}$ months old, and nine were less than 6 months of age; nineteen were between 6 and 12 months, making twenty-eight infants under 1 year who died of tuberculous meningitis, or 38 per cent. of the

tuberculous cases less than a year old in this series. During the second year of life there were twenty-two cases of tuberculous meningitis, or 36 per cent. of the children between 1 and 2 years old having tuberculosis developed meningitis.

TABLE 3.—AGE OF PATIENTS WITH TUBERCULOUS MENINGITIS

2½ months old.....	1	} Under 6 months, 9.	} 28 under 1 year.
3 months old.....	3		
4 months old.....	1		
5 months old.....	4		
6 months old.....	3		
7 months old.....	3	} Between 6 and 12 mos., 19.	
8 months old.....	5		
9 months old.....	2		
10 months old.....	4		
11 months old.....	2		
12 months old.....	2	} Between 12 and 18 mos., 12.	} 22 between 1 and 2 years.
13 months old.....	5		
14 months old.....	1		
16 months old.....	2		
17 months old.....	2		
18 months old.....	4	} Between 18 and 24 mos., 10.	
19 months old.....	1		
20 months old.....	1		
21 months old.....	3		
22 months old.....	1		
Total under 2 years.....			50
2 years old.....	12		
3 years old.....	3		
4 years old.....	3		
5 years old.....	1		

A closer study of these cases of tuberculous meningitis is interesting. The comparative frequency with which children under 2 years of age died of meningitis was about the same throughout both halves of the first year (39 per cent. and 38 per cent.), falling to 33 per cent. in the first half of the second year and rising to 40 per cent. during the second half of the second year. In the entire third year of life our series showed that 43 per cent. of children of that age afflicted with tuberculosis died of meningitis. After the third year our numbers were too few to be of value.

The distribution of the lesions in these cases shows that the younger infants tend to have a larger number of viscera involved in the tuberculous process, while in the older children meningitis may follow a very limited infection. Thus the only child which had tuberculous meningitis and but one other tuberculous focus in the body was 27 months old. Five children showed three other tuberculous lesions besides the tubercles in the pia mater, and they were 2 and 4 years old, respectively. No child under 2 years had less than four other tuberculous organs besides the pia mater, only one child under 1 year presented less than five, and no child under 6 months had less than six other tuberculous organs. The largest number of organs involved

was ten, in infants 3 and 5 months old, respectively. Tuberculous lesions in nine organs occurred in two infants 3 months of age. There were eight children with lesions in eight organs, and of these five were under 1 year of age, the other three ranging from 12 to 21 months. Of twenty children presenting seven tuberculous organs besides the pia mater, thirteen were under 1 year, five between 12 and 18 months and two over 3 years of age. To sum up.

Of 14 children with 5 organs involved	1 was under 1 year of age.
Of 15 children with 6 organs involved	5 were under 1 year of age.
Of 20 children with 7 organs involved	13 were under 1 year of age.
Of 8 children with 8 organs involved	5 were under 1 year of age.
Of 2 children with 9 organs involved	2 were under 1 year of age.
Of 2 children with 10 organs involved	2 were under 1 year of age.

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Of 2 children with 4 organs involved	2 were between 1 and 2 years.
Of 14 children with 5 organs involved	7 were between 1 and 2 years.
Of 15 children with 6 organs involved	5 were between 1 and 2 years.
Of 20 children with 7 organs involved	5 were between 1 and 2 years.
Of 8 children with 8 organs involved	3 were between 1 and 2 years.

22

One child with 1 organ involved	was over 2 years old.
Of 5 children with 3 organs involved	5 were over 2 years old.
Of 14 children with 5 organs involved	6 were over 2 years old.
Of 15 children with 6 organs involved	5 were over 2 years old.
Of 20 children with 7 organs involved	2 were over 2 years old.

19

It will readily be seen that the younger infants have a more generalized tuberculosis and the older children a more localized infection. In other words, the younger infants tend to be overwhelmed by the tubercle bacillus, and no immunity develops. In children over 2 years of age there is an increasing tendency toward immunity and consequent limitation of the lesions for a time. The method of infection of the pia mater is undoubtedly by way of the blood-serum.

The most generalized cases had tubercles in the skin, myocardium, peritoneum, mesenteric glands, intestines, kidneys, liver, spleen, bronchial glands, lungs and pia mater. This occurred in two infants, 3 and 5 months of age.

Of these sixty-nine cases of meningitis, three were of intestinal origin: a child of 2 years with tuberculous peritonitis without lung or bronchial gland involvement, another of the same age without lesions in the lungs, but with cheesy degeneration of a bronchial lymph-node, and a child of 21 months with tuberculosis of the lungs and bronchial nodes as well as of all the abdominal viscera.

Whether the bovine type of tubercle bacilli would have been found in the pia mater in these three cases, especially in the one without any

involvement of the thoracic viscera, is an interesting point. Park⁵ found two cases of tuberculous meningitis due to the bovine type of tubercle bacillus and two have been found by other observers. Certainly meningitis is far less common among cases of tuberculosis of digestive origin than it is in those following respiratory infection, the proportion in our series being 3 to 17 and 67 to 146, respectively, or 17 per cent. of the digestive cases as compared with 46 per cent. among those due to inhalation of the tubercle bacillus.

In one case meningococci were found in the cerebrospinal fluid during life, and the tubercles were found only at autopsy, the purulent condition of the fluid and the presence of meningococci having dominated the clinical picture, so that a tuberculous complication was not considered.

In another case, tubercle bacilli and influenza bacilli were both present in the fluid, and at post-mortem examination a purulent exudate was found over the cortex of both hemispheres, with tubercles in the pia over the cortex and base. This case has been reported by Dr. Faber.⁶

Solitary tubercles in the cerebral hemispheres were present in two cases, one of which had a cheesy mass in the right occipital lobe, another in the right frontal lobe and a third in the cerebellum. These tubercles measured 1 to 1.5 cm. in diameter, and in consequence the lesion in the brain was as extensive as that in the lungs.

YOUNGEST PATIENTS

It is interesting to note that our series comprises two infants who were but 2½ months old. In one of these the mother was tuberculous and the child died of tuberculous meningitis, showing at autopsy a generalized infection involving eight organs, with cheesy pneumonia in one lung.

In the other case the father was dying of pulmonary tuberculosis at the time of the child's admission. Autopsy on this infant showed tubercles in the lungs, liver, spleen, kidneys, intestines, mesenteric and bronchial lymph-nodes. Both these cases were of respiratory origin.

Six children were 3 months of age, and of these three died of tuberculous meningitis. In one the tuberculous infection followed circumcision, and the inguinal lymph-nodes were large and cheesy. In the other five young infants the primary lesion was in the lung and was accompanied by generalized infection. The myocardium con-

5. Park and Krumweide: *Collected Studies from the Laboratories, Board of Health, New York*, 1912-13, vii, 88.

6. Faber, H. K.: *A Case of Tuberculous Meningitis Complicated by Influenzal Meningitis*, *AM. JOUR. DIS. CHILD.*, 1914, viii, 150.

tained one or two tubercles in two of the six infants 3 months old, while in the entire series of 178 cases the heart muscle was involved only ten times; which further proves the tendency to generalization of infection in these young infants.

DISCUSSION

The largest number of our cases were of inhalation origin, as shown by the large percentage of cases in which the pulmonary lesions were the most advanced in the body. The absence of tuberculous lesions from the lungs in fourteen cases and the presence of tuberculous lesions in the bronchial lymph-nodes in seven of these seems to show that it is possible for the tubercle bacillus to pass through the lungs without localizing there.

The inhalation origin of the majority of cases of tuberculosis corresponds with the findings of A. Ghon,⁷ who analyzed 184 cases and found the primary lesion in the lung in all but fourteen. These cases, however, comprise children up to the age of 14, and he does not state what percentage of them were less than 3 years old. Therefore, our results are not really comparable.

It seems to us that Ghon is stretching a point in his discussion of these fourteen cases when he says that while he was unable to find a pulmonary lesion in seven, he prefers to consider that he overlooked it rather than that it was not there. We prefer to look on similar cases in our series as primary localization in the bronchial glands, the tubercle bacillus having passed through the lung without localizing there. We must agree with Ghon's final conclusion that in children the primary infection of the lung is the usual mode of infection, for 82 per cent. of our cases were of this type.

The marked tendency to rapid and general dissemination of the tuberculous lesions throughout the body in infants less than a year old is well shown. In view of that fact the survival of any young infant infected with tuberculosis for more than six months after infection is very remote, while healing of tuberculous lesions in young infants is practically out of the question. In our entire series not a single healed tuberculous lesion was encountered, and attempts at healing, shown by calcified areas, were found only five times in the lung and thirteen times in lymph-nodes. Only twice was it found among infants less than a year old, and in both these cases the extensive generalization of tubercles throughout the body gave evidence that the small calcareous areas present did not prevent spreading of the infection.

7. Ghon, Anton: *Der primäre Lungenherd bei der Tuberkulose der kinder*, Urban and Schwarzenberg, Berlin and Vienna, 1912.

Encapsulation of a tuberculous lesion was not encountered in this series of cases.

The predominance of respiratory over deglutition infection is indirect evidence of the quality of our milk-supply, though it must not be forgotten that children may carry tubercle bacilli into their mouths by means of fingers infected by contact with dirty floors and furniture, as well as by means of food.

The comparative frequency of tuberculous meningitis in young infants is noteworthy, as evidence of the very general dissemination of tuberculous lesions in these young subjects.

The smaller proportion of cases of tuberculous meningitis among the children who acquire tuberculosis by ingestion as compared with those who become infected by inhalation, is in keeping with the fact that the deglutition cases show rather less tendency to generalization than do the respiratory cases.

325 Central Park West—44 East Sixty-Third Street.

RECURRENT MENINGITIS, DUE TO LEAD, IN A CHILD OF FIVE YEARS *

HENRY M. THOMAS, M.D., AND KENNETH D. BLACKFAN, M.D.

BALTIMORE

The case was seen in Dr. Howland's service in the Harriet Lane Home of the Johns Hopkins Hospital. It was that of a boy, between 5 and 6 years old, who was admitted Aug. 22, 1913, having been transferred from the Home of the Friendless in a state of coma.

Little was learned of his early history except that he had had in the eight preceding months two attacks of otitis media, and that for two years he had been subject to rather frequent and severe bleedings from the nose.

He seemed as well as usual up to five days before admission, when he began to complain of pain in his face and head, to be restless at night, and to look ill. The next day stiffness of the neck was noted, and the child vomited on several occasions. He became rapidly worse, and convulsions and coma developed the day before he was brought to the hospital.

On admission he was comatose. His head was retracted, and his arms and legs were extended and spastic. Kernig's sign was, however, not present. There were recurrent, general convulsions. The left eye was deflected inward. The child's temperature was practically normal. There was a leukocytosis of 27,600.

Spinal puncture was done on four occasions—directly after admission, the next day, then in three days, and after an interval of two weeks. The results of these punctures were all very similar, except that the pressure, which was very high on the first occasion, was not above normal on the subsequent punctures. The fluid was always clear and sterile. It contained from twenty to forty cells, mostly mononuclear. It was positive to the Noguchi globulin test, reduced Fehling's solution, and the Wassermann reaction was negative.

The von Pirquet skin test was negative.

The right optic nerve was swollen and its edges obscured. There were numerous hemorrhages in the retina about it. The left optic nerve was practically normal. As noted on admission, the left external rectus was weak. There was nothing else abnormal discovered in the nervous system.

The convulsions, the rigidity of the neck, the optic neuritis, and the spinal fluid findings, suggested a meningitis. It was considered to be a serous meningitis of unknown cause.

Improvement began after the first lumbar puncture, and in a week the patient seemed nearly well, complaining only of headache at night, abdominal pain, and occasionally vomiting. He was discharged September 20, after an examination which revealed nothing abnormal. The spinal fluid, however, showed an increase in the cells and a positive globulin test. The right optic nerve was reported by the ophthalmological department to be quite normal, although there was some difference of opinion in regard to this.

The child was returned to the care of the Home of the Friendless, but was seen from time to time in the out-patient department. The condition remained excellent for five months.

In January, 1914, he had a number of attacks of epistaxis, for which he was treated in the throat department.

* Read at the Annual Meeting of the American Neurological Association held at Albany, New York, May 9, 1914.

On March 1 he began to suffer from headache and vomited. The convulsions recurred and in two days he was again in coma. He was readmitted to the Harriet Lane Home on March 3, in a condition which was almost identical to that of his first admission, six and a half months before. The neck was stiff but there was no definite Kernig sign, and the limbs were not held so stiffly as on the former admission. There was choked disk on the right side, with some retinal hemorrhages; on the left side the disk was sharp-cut—indeed, looked slightly atrophic. He had moderate anemia, hemoglobin of 55 per cent., red blood-cells 4,480,000, white blood-cells 23,100. Lumbar puncture yielded fluid very similar to that found at first admission. The fluid, however, did not seem to be under any noticeably increased pressure.

The recurrence of such a condition naturally aroused a great deal of interest, and the case was studied most carefully from every side. Nothing, however, was discovered that threw light on the etiology, until our attention was attracted to a slight discoloration about a tooth, and a more careful inspection revealed the presence of a very fine but typical lead-line on the gums surrounding many of the teeth. The blood showed well-marked stippling of the red cells (Grawitz's granules), and confirmed us in our view that poisoning by lead was the cause of the trouble.

The urine was examined but no lead was demonstrated in it.

We were much puzzled as to the source of the lead, until he was found with his mouth covered with white lead paint which he had bitten from the railings of his crib. Before this discovery we had investigated the conditions and the other inmates of the institution in which he lived and had found nothing that aroused our suspicion, but the fact that the white paint on the patient's bedstead in the dormitory was chipped off much more than from the others.

After we knew of his peculiar habit, we found that he would gnaw any painted object unless he was most carefully watched.

In this second attack he developed a weakness of the external rectus muscle—this time of the right eye—three or four days after his entrance to the hospital, and he complained from time to time of abdominal pain.

The patient again made a remarkably quick and uneventful recovery. He was discharged on May 1, having been up and around the ward for more than a month, quite recovered except for the persistence of an increase in cells and positive globulin reaction in the spinal fluid.

He remained in good health for three weeks when on May 25 he had a severe convulsion and died. No post-mortem examination was obtained.

Lead-poisoning in children does not seem to be very common, although it is well recognized. That there is a special form of meningitis due to lead has been insisted on only by the French observers. That lead affects the central nervous system has been long known, and in certain fatal cases of lead encephalopathy anatomic changes have been noted in the meninges together, at times, with increase of the fluid in the ventricles or in the subarachnoid space. Felix Aussendorf¹ has collected reports of a number of such cases, among them Spiller's² important case.

French clinicians, true to their historic interest in lead poisoning, have, in the last ten years, been much occupied as to the effects of the metal on the brain and its coverings. Among the numerous articles

1. Aussendorf, Felix: Zur Kenntnis der pathologischen Anatomie des Zentralnervensystems bei Encephalopathia saturnina. Inaug. Diss., Leipsic, 1911.

2. Spiller: Jour. Med. Research, August, 1903, x, No. 1.

those written by Mosny, in association with several collaborators, are the most important. In the chief of these, Mosny and Malloizel³ give the histories of forty-seven cases of lead-poisoning, mostly from their own experience, in almost all of which lumbar punctures were done and the cerebrospinal fluid studied.

They point out that in acute lead colic there is very generally evidence of involvement of the meninges as shown by the fact that the cerebrospinal fluid contains an increased number of cellular elements, mostly lymphocytes. In these so-called abortive cases (*la méningite fruste*) the only symptom of such meningeal irritation may be headache, but the severity of this is not always proportionate to the laboratory findings.

In chronic lead-poisoning they rarely found any change in the cerebrospinal fluid.

In other cases classed as acute lead meningitis, the symptoms of involvement of the central nervous system are pronounced. In these the meningeal reaction, as revealed by lumbar puncture, is always very marked, persistent, and may be as intense as in tuberculous meningitis. It is in this group that our case would be classed, together with many cases of the so-called lead encephalopathy.

Mosny and Malloizel feel that the term "lead encephalopathy" is far too general, and they have attempted to divide the cases into more definite clinical groups, in all of which, however, there is more or less evidence of involvement of the meninges, as shown by the results of spinal puncture.

It is to be regretted that there is no record in their excellent article of any ophthalmoscopic examination.

Plate⁴ reports a typical clinical case of lead meningitis in a young man of 20. Four lumbar punctures were done, giving a decreasing cell-count from 90 to 14. The author thinks his is the first case reported in Germany.

Mass⁵ reports a number of cases in which the diagnosis of acquired hydrocephalus, due to serous meningitis, was made, and in which he thought he could assume lead as the cause. These cases were seen in the chronic stage or at necropsy, and in none of them was lead proved to be more than a possible etiological factor.

Involvement of the optic nerves and of the motor nerves of the eyeballs in the course of lead-poisoning, although certainly not fre-

3. Mosny and Malloizel: *La méningite saturnine*, 1907, xxvii, 506.

4. Plate: *Ueber einen Fall von Meningitis saturnina*, München. med. Wehnschr., 1913, lx, 2343, 2345.

5. Mass: *Ueber eine besondere Form der Encephalopathia saturnina (Meningitis serosa)*, Monatschr. f. Psychiat. u. Neurol., 1911, xxx, 207.

quently noted in America, is well known. Wilbrand and Saenger⁶ have collected reports of most of the cases. It would seem that optic neuritis may occur primarily, or through the direct toxic action of lead on the nervous system, or by the production of interstitial neuritis, or through the alterations of the blood-vessels in the retina and optic nerves, or secondarily through intercranial changes or changes in the kidney. Paralysis of one or more of the external eye muscles is not infrequently associated with optic neuritis, or may occur alone.

J. Lockhart Gibson⁷ has for a number of years repeatedly called attention to a most remarkable group of cases seen in children of Queensland, Australia. The case which we have reported seems closely allied to these. In that country children in general seem peculiarly liable to lead-poisoning, and perhaps especially to its effects on the eyes. Gibson has seen as many as nine cases of what he calls plumbic ocular neuritis in a single year. This condition usually affects children below the age of 8, and is characterized by the development of squint, due to weakness of one or both external recti, and associated with marked optic neuritis. There is often no other symptom of lead-poisoning, but at times more serious symptoms of lead encephalopathy are present. Gibson believes the source of the lead to be usually due to the children's getting dried paint from the railings of long-painted verandas or garden fences on their hands and then into their mouths. Children who suck their fingers or bite their fingernails are more liable to the disease. He regards the condition as a neuritis, but points out in his last article the great importance of an early lumbar puncture, and the almost constant finding of an increased pressure in the cerebrospinal fluid. He regards the withdrawal of the fluid as the essential therapeutic measure, surely indicating that meningeal irritation must be an essential factor in the condition.

We have found no record of any examination of the withdrawn fluid, either chemically or microscopically.

The case which we have reported, the results of lumbar punctures in acute lead colic, the results of certain of the autopsies of patients dying of lead encephalopathy, the cases reported by Gibson, all force us to the conclusion that lead appears to have a special effect on the meninges and the central nervous system, and that it may not infrequently be the unsuspected cause of so-called serous meningitis.

1228 Madison Avenue—Johns Hopkins Hospital.

6. Wilbrand and Saenger: *Die Neurologie des Auges*, 1913, v.

7. Gibson, J. Lockhart: *Australian Med. Gaz.*, 1897 to 1912; *Brit. Med. Jour.*, 1908.

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INFANTILE SCURVY: THE BLOOD, THE BLOOD-VESSELS AND THE DIET *

ALFRED F. HESS, M.D., AND MILDRED FISH
NEW YORK

The following study considers infantile scurvy from a point of view which is somewhat unusual. Although it includes a chapter on diet, it is nevertheless chiefly concerned with scurvy as a hemorrhagic disease. This phase of the subject seemed worthy of investigation, as hemorrhage is the typical clinical symptom of scurvy, whether it manifests itself in bleeding into the gums, or as the equally well-recognized subperiosteal hemorrhages of the long bones. Indeed, some authors follow Barlow in considering infantile scurvy under the group of the hemorrhagic diseases, believing the hemorrhages to be the primary disturbance. There has been, however, as far as we know, no study of the blood in this disease, if we except some estimations, scattered through the literature, of the hemoglobin or of the blood-cells. We have devoted our attention especially to the question of the coagulability of the blood, with the object of ascertaining whether there is any marked change in this particular and whether a disturbance of this function can account for the various hemorrhagic symptoms. As it is now known that coagulation is closely associated with the platelets of the blood, an examination of these cells was also carried out. In addition a routine examination was made of the red and the white blood corpuscles and of the hemoglobin. In the course of this study our attention was gradually directed from the blood to the blood-vessels. We found it urgent to seek some means by which we could distinguish between hemorrhages due to a weakness of the blood-vessels and those which are the result of some defect of the blood itself.

As may be supposed, no intimate study of this kind could be pursued without having interesting clinical phenomena present themselves for consideration from time to time. We shall not, however, consider infantile scurvy from a clinical point of view, as the disease has been so frequently and thoroughly treated in all its symptomatology, but

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* From the Research Laboratory, Department of Health, New York City.

shall merely discuss a few clinical phenomena which seem to be of interest. The same is true as regards diet. This question will also not be taken up in detail, but be discussed merely in some particular aspects. Our study in the main is based on numerous cases of scurvy which have developed in the past few years in the Hebrew Infant Asylum. We are dealing, therefore, with a group of institutional infants concerning whom we have clinical records for a long period previous to the onset of the disease, and whose welfare we have been able to follow for many months following their recovery. A number of these cases developed in the course of an attempt to dispense with the giving of orange-juice. In view of the fact that pasteurized milk is now heated to a temperature of only 145 F., which is claimed by many (including the commission on milk standards) not to destroy its chemical constituents, it seemed that infants should thrive on this milk without the addition of fruit-juices to their diet.

In obtaining blood for the tests of coagulability, about 5 c.c. was obtained from the jugular vein and allowed to flow into a 1 per cent. solution of sodium oxalate in the ratio of 1:10. In no case were coagulation tests made from blood obtained from the prick of a finger or the lobe of the ear; these methods cannot be relied on, as they introduce the disturbing factor of the thromboplastic substance of the tissue juices, and thus do not allow us to obtain an accurate estimate of the coagulability of the blood itself. The importance of this point may be realized when we add that the simple fact of not entering a blood-vessel at the first attempt, and in this way of introducing a minimal amount of tissue-juice into the aspirated blood, was found to invalidate our results. The oxalated blood was immediately centrifuged for fifteen minutes at high speed, and the plasma pipetted off for examination. The coagulation tests were carried out after the method suggested by Howell,¹ which is as follows:

Five drops of plasma are added to each of five small test-tubes. To these tubes increasing amounts (one to five drops) of 0.5 per cent. calcium chlorid made up in normal salt solution are added. The time is then noted when the plasma in the various tubes is firmly clotted. This time is designated as the coagulation time, and was noted in our records (Table 1) by a +++ sign. Lesser degrees of coagulation were marked +, which indicates the very faintest beginnings of coagulation, and ++ which indicates a jellylike consistency of the clot.

In addition to these tests, a test was made for antithrombin in many cases. For this purpose, the plasma was heated to 60 C. in order to destroy the prothrombin, and was then filtered, in order to get rid

1. Howell, W. H.: The Condition of the Blood in Hemophilia, Thrombosis and Purpura, *Arch. Int. Med.*, January, 1914, p. 76.

of the coagulated fibrinogen. One drop of this heated plasma was put into each of four tubes. To these tubes 1, 2, 3 and 4 drops, respectively, of thrombin was added. This thrombin was prepared from fibrin after Howell's method and was obtained in crystalline form. After the antithrombin and the thrombin had remained in contact for

TABLE 1.—RESULTS OF COAGULABILITY TESTS OF PLASMA (PROTHROMBIN)

Date	Name	CaCl ₂ 0.5 % (drops)	Time of Coagulation (min.)*	Remarks
4/3	M. N. (scurvy).....	1	12	Infant has hemorrhage into the gums and petechiae on body.
		2	10	
		3	9	
		4	9	
		5	9	
	A. B. (normal).....	1	7	
		2	6½	
		3	6½	
		4	6½	
		5	7	
5/4	M. H. (scurvy).....	1	15+	Infant has slight peridental hemor- rhage and some petechiae.
		2	10	
		3	10	
		4	10	
		5	10	
	C. F. (normal).....	1	15+	
		2	15+	
		3	10	
		4	10	
		5	8	
	B. B. (scurvy).....	1	15+	Infant has swelling of femur.
		2	15+	
		3	12	
		4	8	
		5	8	
5/15	H. G. (scurvy)....	2	15+	A freshly made solution of calcium was used in this experiment. A mild case of scurvy.
		3	14	
		4	12	
		5	12	
		6	10	
		7	14	
	S. B. (normal).....	2	15+	
		3	10	
		4	10	
		5	10	
		6	6	
		7	10	
	H. C. (scurvy).....	2	15+	A mild case of scurvy.
		3	12	
		4	12	
		5	10	
		6	8	
		7	12	

* Five drops of oxalated plasma.

EPICRISIS.—In these tests the tube which first showed clotting should be taken as the standard, as it represents the optimal recalcification. It will be noted that coagulation was but slightly delayed in the cases of scurvy.

fifteen minutes, ten drops of a fibrinogen solution (made from cat plasma) were added and the time noted when coagulation occurred. In all these tests, whether for prothrombin or for antithrombin, control tests of normal plasma were carried out at the same time and under identical conditions.

Table 1 shows five tests of plasma from scurvy and three from control cases. It will be seen (Table 2) that two kinds of examinations were made; the one, which may be termed the coagulability test, includes the interaction of all the substances of the plasma, the prothrombin, the antithrombin, the calcium, the fibrinogen, etc., and the other, designated as the antithrombin test. Looking over Table 1 we

TABLE 2.—RESULTS OF EXAMINATIONS FOR
ANTITHROMBIN

Date	Name	Thrombin (Drops)	Time of Coagulation (Min.)
4/3	M. N. (scurvy).....	1	16
		2	4
		3	3
		4	3
	B. G. (child who frequently developed ecchymotic spots)	1	14
		2	5
		3	3
		4	3
	A. B. (normal)	1	20
		2	6
		3	5
		4	5
5/4	M. H. (scurvy).....	1	26
		2	6
		3	6
		4	6
	C. F. (normal).....	1	20
		2	6
		3	6
		4	6
	B. B. (scurvy).....	1	14
		2	4
		3	4
		4	4

EPICRISIS.—Evidently the antithrombin is not increased in scurvy; further tests confirmed these results.

find that the plasma of the scurvy cases generally clotted more slowly than that of the controls; in other words, that there is a slightly diminished clotting-power of the blood in scurvy. This property, however, is not absolutely constant, and therefore not an essential manifestation of scurvy. To what constituent of the blood is this diminished coagulability to be attributed? A glance at Table 2 at once negatives the possibility that it may be occasioned by an increase of antithrombin. The tests were uniformly convincing in this regard. May it then be the result of a lack of prothrombin or a lack of calcium or a deficiency of both these essential factors of clotting?

The question of a deficiency of calcium in the blood is an interesting one, not only because this substance is of prime importance in coagulation, but in view of the fact that some have maintained, as we shall see, that the calcium content is decreased in the tissues in scurvy, whereas others have found it to be increased. Before discussing this question, however, let us consider the significance of these coagulation tests from this point of view. The addition of sodium oxalate to plasma prevents clotting, as is well known, by means of precipitating the calcium in the blood. It should be understood that in the ratio in which we have added it to the plasma, it is not sufficient to precipitate all the calcium in the blood, some calcium still remains in solution. This becomes evident if we compare the results of adding the usual strength (1 per cent. of oxalate) and twice this percentage to specimens of the same blood.

Table 3 reproduces an experiment of this kind. This table shows that although there is no difference as to time of clotting between the series to which 1 or 2 per cent. oxalate was added, there is marked difference between them as regards the tube in which the clot first occurred. In the tests in which 1 per cent. sodium oxalate was added, there was rapid clotting when 3, 4 and 5 drops of calcium solution were added to the plasma. On the other hand, where the plasma had been made with a 2 per cent. oxalate solution it required 5 drops of the calcium solution to recalcify the plasma sufficiently to bring about a clot; 3 or 4 drops of calcium were absolutely insufficient to bring about this result. In other words, the clotting-time remains unaltered in our tests whether we add more or less of the sodium oxalate solution; the only difference is that, if we add more oxalate, it is necessary to recalcify with a correspondingly greater number of drops of the calcium solution. There is one other physiologic fact which we must take into consideration in judging these coagulation tests, namely, that in the clotting of the plasma the amount of calcium necessary to produce a clot varies in direct ratio with the amount of prothrombin present. It is therefore not correct to consider these two factors separately — to

speak, for instance, of a deficiency of calcium; for it is only a relative deficiency that has any clinical importance. If the plasma is diluted to one-half, less calcium is required to produce a clot; if it is diluted to one-fourth, still less calcium is required. We shall not enter into the details of the experiments which demonstrate this interesting phenomenon, as we expect to report on it elsewhere in another connection.

With these facts before us as regards both the decalcification of plasma by oxalate and the interrelation of calcium to prothrombin in the clotting process of the blood, let us return to Table 1 and consider whether it can furnish any information as to a possible deficiency of

TABLE 3.—COAGULATION TEST OF PLASMA PREPARED WITH A WEAK AND A STRONG OXALATE SOLUTION

Date	Strength of Oxalate Added (%)	CaCl ₂ 0.5 % (drops)	Time of Coagulation (min.)*	Remarks
6/26	1	1	36+	Both tests were made with the same specimen of blood.
		2	36+	
		3	7	
		4	6	
		5	6	
	2	1	36+	
		2	36+	
		3	36+	
		4	36+	
		5	6	

* Five drops of oxalated plasma.

EPICRISIS.—The strength of the oxalate solution does not affect the time of clotting, but does influence the amount of calcium which it is necessary to add in order to bring about coagulation. The calcium is therefore not entirely precipitated from the blood by the 1 per cent. solution.

these two substances. Although it does not enable us to state whether or not there is a slight decrease of prothrombin, it does enable us to judge whether or not a *relative* deficiency of calcium exists, that is to say, relative to the prothrombin. From a physiologic standpoint, as we have stated, this is the only type of calcium deficiency that is important — a condition of negative calcium balance, in which the calcium is insufficient to bind all the prothrombin, and in which, as a consequence, coagulation is retarded. Such a condition does not exist in infantile scurvy. *The slight defect in coagulability cannot be attributed to a relative insufficiency of calcium.* Had such been the case, we should have found it necessary to add an increased amount of calcium to the

plasma in scurvy cases as compared with the normal control; the clotting would have occurred in the tubes containing the larger amounts (five or six drops) of calcium solution. The tests show, however, that no increased addition of calcium was necessary. Whatever may be the finer physiologic cause, the slight defect in the clotting-power of the blood, which we have noted, plays but a secondary rôle in this disease; the characteristic hemorrhages are the result, as will be shown below, of quite a different pathologic condition.

A few simple tests of coagulation were made with unaltered blood. For this purpose ten drops of blood were dropped from the syringe into thoroughly cleaned, flat-bottomed test-tubes, 1.5 cm. in diameter, and the time of clotting ascertained. The normal coagulation time of blood tested in this manner is about six minutes. The tests of the blood of the scurvy cases varied between four and one-half and eight minutes and were therefore considered to correspond to the tests with plasma.

In addition to the coagulation-time of blood, the bleeding-time has been emphasized, especially by Duke.² This term refers to the time which it takes the blood to cease flowing after a puncture is made into the tissue. For this purpose a prick may be made in the lobe of the ear and the time noted when the blood ceases to flow. It is evident, according to what we have stated above, that a test of this kind includes at least two factors of coagulation, the coagulability of the blood as well as the thromboplastic substances of the tissues, and therefore that it is not identical with a test of the coagulation time of the blood or of the plasma. In two cases, one mild, the other pronounced, there was found to be a prolonged bleeding-time. The blood kept flowing from the puncture for fully five minutes and showed a deficiency in clotting. In other cases, however, in which the disease seemed equally advanced a prolongation of the bleeding-time was not met with, so that we must conclude that this abnormal condition may occur, but cannot be considered characteristic of the disease.

Table 4 shows the result of the examination of platelets. These tests were carried out by means of the staining solution recommended by Wright and Kinnicutt, the blood being obtained from the finger-tip. Although we were unable to obtain uniform counts from day to day, nevertheless the number of platelets was found in all cases to fall within normal limits. There was no marked decrease in the number of platelets such as has been described in connection with some hemorrhagic conditions and which might account for a tendency to hemorrhage. It will be noticed that in each case two counts were carried out.

2. Duke, W. W.: The Pathogenesis of Purpura Hemorrhagica with Especial Reference to the Part Played by Blood-Platelets, *Arch. Int. Med.*, November, 1912, p. 445.

In other particulars the blood shows the changes which are commonly associated with secondary anemia (Table 4). There was a relative as well as an absolute deficiency in the hemoglobin, a slight decrease in the number of red blood-cells, occasionally the appearance of a nucleated red cell, and an increase in the number of leukocytes.

TABLE 4.—THE PLATELETS AND OTHER BLOOD-CELLS IN SCURVY

Name	Date	Plate-lets	Leuko-cytes	Erythro-cytes	Hmgl. % (Sahli)	Remarks
M. H.	5/ 3	280,000	
	5/ 4	248,000	10,000	
	5/ 5	Boiled orange juice given.
	5/ 8	4,300,000	35	
	5/16	15,900	
	7/ 2	6,800	5,456,000	40	Well but pale.
A. L.	5/ 3	300,000	
	5/ 5	21,000	
	5/ 9	5,480,000	..	
	5/11	382,000	
	5/13	65	
	5/16	11,500	
H. C.	5/ 8	320,000	20,000	
	5/ 9	5,340,000	..	
	5/13	70	
	5/16	362,000	
B. B.	5/ 4	496,000	21,000	A severe case.
	5/13	585,000	14,000	3,200,000	70	
	5/18	17,600	
	7/13	40,000	7,672,000	82	Has gained well lately.
	7/15	7,640,000	88	
H. Y.	5/15	560,000	
	5/16	424,000	
	7/ 9	5,750,000	45	

It is impossible to state whether this moderate leukocytosis has any specific connection with the disease, or whether it is a reaction to some toxic substance existing in the circulation and should be brought into relationship with the slight febrile reaction which has been frequently noted to occur as one of the phenomena of infantile scurvy. In connection with these blood-changes we wish to call attention to the

regeneration of hemoglobin and of red cells during the convalescence of the disease. It will be noticed (Table 4) that in one instance there was an abnormal increase in the red cells (polycythemia), the count reaching over seven millions on two successive days.

THE BLOOD-VESSELS: CAPILLARY RESISTANCE TEST

What then is the cause of the bleeding which dominates the clinical picture of this disease? When it was found that the hemorrhages could not be accounted for by a defect in the clotting-power of the blood, we directed our attention to some disturbance of the blood-vessels. For the purpose of this investigation we devised a "capillary resistance test,"³ which is carried out as follows:

A blood-pressure band is placed about the infant's arm in the usual manner. We made use of the Tycos apparatus for this purpose and raised the pressure rapidly until it reached the 90 mark. After the pressure had been maintained at this level for three minutes the band was removed, and when the blueness of the arm had faded an examination was made for petechial spots. The principle of this test is simple and must be evident at once. It consists merely in putting an excess of pressure on the capillaries and venules and observing whether the vessels allow the blood to escape readily. Ninety degrees pressure was selected as the optimum, because it was found that a less degree did not regularly produce venous congestion of the arm, which it is essential to bring about. In a few cases, due to an unexplained cause, there was an increase of arterial pressure reaching 100 or somewhat higher, so that raising the resistance to 90 did not produce cyanosis of the extremity; in a case of pertussis the pressure reached 125 when the infant cried. In such cases it was of course necessary to raise the pressure somewhat higher, as the entire test loses its efficacy if the return flow of the blood is not completely occluded. Numerous cases of scurvy were tested by this means and in addition, many normal cases served as control observations. It was found beyond question that the scurvy cases reacted abnormally. In these infants the forearm would show many petechiae; in some cases they were sprinkled over the entire surface whereas in normal infants they were almost always absent or there were but few to be seen.⁴ In the case of an infant 18 months old, who developed a mild scurvy

3. Hess, A. F.: *Proceed. Soc. Exper. Biol. and Med.*, 1914, xi, 130.

4. No importance should be attached to the petechiae which appear just below the pressure band, as these are found in most cases, normal as well as abnormal. After removing the bandage a sufficient interval should be permitted to elapse for the arm to assume its normal color so that the minute hemorrhages can be readily seen. Pressure tends to bring them out prominently. It is probable that the test can be carried out by simply applying a tourniquet for three minutes sufficiently tight to cause venous congestion but not to obliterate the radial pulse.

in spite of receiving vegetables, the test was negative; in all others it was positive, and persisted in some instances after all definite symptoms had disappeared. Where an eruption, such as eczema or prurigo was present on the forearm, the petechiae developed especially at the site of the lesions.

The capillary resistance test is brought forward not as a specific test for scurvy, but rather as a method of bringing to view a weakness of the vessel walls whatever may be the cause. We have found it to be positive in various cases of toxemia, and it will no doubt be found to be present wherever the vessel walls are weak; for example, in some of the purpuras which occur more frequently in adult life.

In connection with scurvy a study of petechiae is of the greatest interest. In our experience they have been present very frequently in the earliest stages of the disease. It is probable that their presence has not been emphasized in descriptions of this disease because they have not been sufficiently sought for. This year we had an exceptional opportunity of investigating this sign, as well as other early symptoms of the disease, when, as stated above, we were making observations on the group of infants fed with milk which had been subjected to a moderate degree of temperature. As may be imagined, not only were petechial spots sought for almost daily, but all other early signs of disturbance of nutrition were examined for with regularity. In adults in the course of various purpuras, superficial petechial spots are found especially in the skin of the lower extremities. This can probably be explained by the fact that these vessel-walls give way as the result of the increased pressure of gravity, brought about by the standing posture. We should naturally expect the distribution of petechiae in infants to be somewhat different on account of their horizontal posture. Such proved to be the case. Petechiae were most frequently seen on the upper part of the back and neck, and on the chest, and more often on the upper than on the lower extremities. There was, however, no part of the body that can be said to have been entirely spared. They were found in the mucous membrane of the hard and soft palate, and also in several instances on the palpebral conjunctiva, appearing just as they do so typically in cases of bacterial infection of the blood. It is probable that we must consider the blood in the urine, especially the minute hemorrhages which can be detected only by microscopic examination, merely as an evidence of petechiae into the internal organs. Post-mortem examinations show the same wide distribution of small hemorrhages. In almost all cases they have been found in the pleura, peritoneum, pericardium, in addition to the large extravasations which are found beneath the periosteum.

Beside the petechial hemorrhages, we must consider edema as being typical of an increased permeability of the vessel-wall. In scurvy we

frequently find not only petechiae but also edema. Edema of the eyelids and of the ankles is well known as a clinical manifestation of the scurvy of infants as well as of adults. Post-mortem examinations also confirm the increased permeability of the vessels in this regard; fluid is commonly found in the pleural, the peritoneal, and the pericardial cavities, as well as a marked increase of fluid (noted on incision) in the subcutaneous tissues.

A comparison of scurvy and hemophilia from this point of view brings out a striking contrast. In hemophilia we do not find petechial spots scattered over the surface of the body, nor is edema a symptom of the disease. On applying the "capillary resistance test" in cases of hemophilia—we have tested three cases of this disease by this method—it is found that petechiae are not induced by this increase of intravascular pressure. In other words, in hemophilia the vessels seem to be normal. The clinical symptoms of the two diseases bring into sharp relief this distinction in the pathogenesis of the hemorrhages. In scurvy the hemorrhages are generally minute and numerous; in hemophilia the hemorrhages are few and extensive, because when the blood does escape from the vessels an excessively large amount is poured out owing to its defective coagulability. We shall not, however, enter on this subject in greater detail, as it will be considered in the future as a study of hemophilia.

When one makes a subcutaneous puncture, for example, into the abdominal wall, in the case of an infant suffering from scurvy, it was found that very often a small hemorrhage develops at the site of the puncture wound. This is not the case when one makes a hypodermic or subcutaneous puncture in a normal person. It was thought that this observation might be of value in distinguishing early cases of scurvy, and, in fact, the first tests carried out with this object in view promised well for this method. In this case (that of an infant, 6 months old, admitted to the asylum in the spring of 1913) puncture tests of this kind resulted in a hemorrhagic reaction; as soon as orange-juice was given the reaction ceased. More extensive trials with this puncture test, however, showed it to be unreliable. This is due partly to the fact that although a minute hemorrhage occurs, it does not always appear at the surface, but is concealed beneath the integument. Notwithstanding the fact that subcutaneous puncture cannot be relied on for diagnosis, it is of interest to note the difference between the reaction to this simple procedure of normal infants and of those afflicted with scurvy; it may prove to be of diagnostic value when hemorrhage results. Possibly it is merely an evidence of increased bleeding-time, or the subcutaneous tissues as well as the vessels may be involved in this disease.

CLINICAL OBSERVATIONS

In a consideration of scurvy the period which may be termed pre-hemorrhagic or prescorbutic is the most important. By this is meant the time when the first nutritional changes take place and before the diagnosis can be made. This interval varies in length according to individual susceptibility and according to the diet which the infant received. In our cases it varied from about four to seven weeks. This prescorbutic period, during which scurvy is latent, frequently passes unnoticed and indeed in many cases does not furnish any sign or symptom whatsoever by which it can be recognized. The question also may be raised as to just when scurvy can be considered cured, and whether there is not a postscurbutic latent period. Are we to consider an infant who has had scurvy normal, as soon as all the signs and symptoms of illness have disappeared? It is probable that although the symptoms of scurvy disappear with almost miraculous rapidity within even a few days of the administration of orange-juice or fresh vegetables, many of the cells of the body do not become normal for a far longer period. This conclusion would follow from the fact that when we apply the capillary resistance test to infants who have had scurvy, we find that they react positively, that the vessels show an abnormal permeability, for some weeks after all symptoms have disappeared. Again, a case such as the following leads us to this opinion:

J. H., April 19, 1913, showed signs of scurvy; the left femur was swollen and tender, also the tibia. There was swelling of one eyelid. These symptoms developed in spite of the fact that breast-milk had been given for eight days previously. On April 19 orange-juice was given. Although the swelling and the tenderness of the bones rapidly disappeared and the child gained in weight and appeared well, it again developed (on May 9) a hemorrhage over one eyelid.

In other words, although the child seemed to be absolutely well, there evidently was still a tendency to hemorrhage. Furthermore, the liability to recurrence or to relapse in scurvy would suggest that the tissues do not return absolutely to the normal state, although this might also be interpreted as evidence of a susceptibility on the part of the individual infant. In the literature recurrences are mentioned as occurring very exceptionally. This view is probably based on the fact that following the development of scurvy, all precautions are taken to prevent a recurrence. During the last few years we have observed two instances in which infants have twice had scurvy; indeed, it seems logical to suppose that, given favorable conditions, a second attack will occur. The following is a case in point:

Infant 6 months old, weighing $10\frac{1}{2}$ pounds in September, 1913, developed swelling above and below the knee, accompanied by marked tenderness. It had been getting Schloss milk for one month. When lemon-juice was given and

the food changed to two-thirds pasteurized milk and one-third barley-water with sugar, the symptoms rapidly disappeared. The lemon juice was discontinued at the beginning of January. Six weeks later tenderness of the lower extremities was noted and a hemorrhagic reaction to subcutaneous puncture. In addition to the milk, the infant had received cod-liver oil and phosphorus for three weeks. Hemorrhage of the gums developed some weeks after this. At the time of the first attack of scurvy, the infant was 6 months old and weighed $10\frac{3}{4}$ pounds; at the time of the second attack it was 11 months old and weighed $14\frac{1}{2}$ pounds.

Although we do not wish to consider the symptomatology of scurvy, as it has been thoroughly portrayed so often, nevertheless we shall devote a few words to the all-important subject of the early symptoms. We have had an exceptional opportunity to observe the disease from this point of view, especially during the past year where, for a time, we were watching a group of infants to ascertain whether they would show any scorbutic signs on discontinuing the giving of fruit-juice. Writers on this subject have described various symptoms as constituting the earliest signs of the disease. Our experience in this regard has been as follows:

In many cases we found the petechial spots, referred to above, as the first evidence of incipient scurvy; the classical tenderness of the extremities was very often called to our attention by the nurse; in other instances the pallor of the infant led to the diagnosis of scurvy. This peculiar pallor has been noted by many observers and has been attributed by some to a loss of blood due to the hemorrhages. This correlation, however, does not seem to exist. The case among our series which had the greatest amount of hemorrhage, a true hematuria, nevertheless did not show marked pallor. It is probable that the loss of color is due rather to some disturbance of nutrition. Loss of appetite occurred early in some cases, but was not a constant feature. In others marked sweating was noted. English authors have laid especial emphasis on the early occurrence of red blood-cells in the urine. In view of this opinion especial attention was given to this point, to determine whether it constituted a reliable sign of the onset of this disease. It was, however, found quite inconstant. In several cases frequent examinations were made of centrifugalized specimens of the urine and no red cells whatsoever found, although at this time there was typical hemorrhage into the gums. In numerous instances we could observe no sign previous to these hemorrhages into the gums, occurring where teeth were present or were about to erupt. In some of these cases the hemorrhage into the gum was posterior to the teeth, and could be seen only when the mouth was wide open. Hemorrhages frequently can be artificially produced by sharp rubbing of the gums, a little expedient which will be found to be of diagnostic value in some cases. The distribution of the hemorrhage depends merely on chance circumstance.

For example, it seems reasonable to ascribe the fact that the subperiosteal hemorrhages involve the femur most frequently, to the frequent handling of the thighs in the course of the diapering of the infant. As has been stated above, almost any region may be involved in the hemorrhage. Not infrequently it may develop over the skull-bones. Finkelstein mentions that hemorrhage has been found post mortem in the dura mater. In one of our cases (L. S.) in which convulsions supervened in the course of the disease, the blood-tinged cerebrospinal fluid led us to believe that we were dealing with a case of this nature. This paragraph may be summarized by stating that there is no symptom which can be considered as preeminently the primary sign of scurvy; each varies in its time of appearance. *We would, however, add to the category of early signs of this disease the development of numerous petechial spots.*

According to our experience, the infectious diseases, including the prevalent infection termed "grip," do not play an essential rôle in the production of infantile scurvy. In 1912 a very severe and extensive epidemic of this infection spread through the infants' ward at about the same time that numerous cases of scurvy developed, but a careful analysis showed that there was no relation between the two diseases. It is probable, however, that any disturbance which decreases the vitality tends in a measure to the development of scurvy. Many of our patients had rickets as well as scurvy. The question of the interrelationship of these two diseases has been discussed pro and con since scurvy was first described by Barlow. In the statistics compiled by the American Pediatric Society, 45 per cent. of the scurvy patients suffered from rickets. In both cases of recurrence of scurvy which occurred in our wards it should be noted that rickets was also present.

Although the relationship between rickets and scurvy is questionable, there is another disease or diathesis which we believe to be definitely associated with the incidence of infantile scurvy. We refer to the condition described by Czerny as "exudative diathesis," a term which implies a predisposition to develop exudations into the skin or the mucous membranes; prurigo, "milk crust," some cases of eczema, recurrent bronchitis, etc., are some of the numerous manifestations of this congenital condition. It is generally agreed that a predisposition to scurvy exists, that although a large number of infants may receive the same diet only a few develop scorbutic symptoms. This has also been our experience in the infant asylum. Closer investigation revealed the fact that *almost all the cases that developed scurvy had exudative diathesis*; this was true in ten of the twelve cases, and in the two exceptions our records are incomplete in this regard. The association was so evident, that we have no hesitation in considering that there is

a close inter-relationship between the two conditions, that *exudative diathesis implies not only a diathesis for exudations, but also for the development of scurvy*. It is impossible to state whether this clinical relationship is one of summation or whether the two pathologic states are dissimilar, the exudative diathesis merely rendering the tissues more vulnerable toward scurvy. In this connection it is probably not without significance that the blood-vessels in exudative diathesis also show a decided weakness, an increased permeability, as judged by the capillary resistance test; petechiae can be produced by pressure in such cases not only during the scurvy, but to a less degree long after the scorbutic symptoms have disappeared.

In order to test the vital activity of the cells in scurvy the Schick test was carried out on six patients. This test consists in injecting intracutaneously 0.1 c.c. of a 1:10,000 solution of diphtheria toxin. In four patients ranging in age from 8 to 13 months there was no reaction; in other words, a sufficient amount of diphtheria antitoxin had been elaborated in the body to neutralize the toxin which was injected; in two cases the reaction was positive. From these tests it would seem that in spite of the marked nutritional changes, the cells are able to elaborate some of the important immune bodies. It would seem that in this disease the functions of certain cells are affected far more than those of others. For instance, the very changes so typical in the bones are brought about by the association of a lack of functioning of the osteoblasts combined with a normal activity on the part of the osteoclasts.

DIET

The infants in the group which we are particularly considering were being fed on various preparations of milk, and their diet was in no wise changed, excepting, as has been stated, that an attempt was made to do without orange-juice. Most of them were receiving mixtures of milk and barley water, the milk being "Grade A Pasteurized," that is, heated for thirty minutes to 145 F. Some were receiving malt soup, others Schloss milk and a few Eiweissmilch. It is interesting to note that all four children who were being fed on malt soup developed scurvy; this may have been mere chance, as these infants all had exudative diathesis, but can also be accounted for by the fact that in the preparation of this food the milk had been heated twice, the pasteurized milk having been brought to the boiling-point. As Neumann pointed out, this two-fold heating probably plays an important rôle in the production of scurvy. It is also possible that the malt should not be disregarded in this connection. Whether cereal, which was used in the form of barley-water, tends to the production of scurvy has never been definitely determined. This point must be borne in mind, how-

ever, in view of the classical paper of Holst and Froelich⁵ on experimental scurvy produced by the giving of cereals, and on reflecting how large a part proprietary foods played in the statistics of the American Pediatric Society. As regards the cases which developed on an Eiweissmilch diet, little need be added. This is not a criterion of the efficacy or usefulness of this food, which was devised not as a permanent diet, but as a therapeutic agent.

During the past three years we have had a considerable number of cases of scurvy develop in infants being fed on pasteurized milk. In 1912, when the first cases were noted, we were pasteurizing the milk in our own diet kitchen, heating it to a temperature of 165 F. for twenty minutes. At this time several cases of scurvy developed, owing to the fact that through an oversight orange-juice was not given. During the past year we have been supplied by one of the large dealers with a pasteurized milk that has been heated only to 145 F. for thirty minutes. Nevertheless, we had several cases of scurvy develop on this diet. In most of the cases the infant was receiving two-thirds milk and one-third barley-water, with the addition of sugar. In two instances, whole milk was being given without the addition of barley water. There were other patients in the same ward on the identical diet who did not develop scurvy. In other words, the pasteurized milk was not the sole factor in the production of the disease. That the pasteurization did play an important rôle, however, was shown by substituting raw, unheated milk for the pasteurized milk, the formula and the amount of food remaining unchanged. In this case the scorbutic symptoms began to disappear within a week of giving raw milk and had altogether vanished in two weeks. Whatever the predisposing factor of scurvy (this infant had exudative diathesis), a case with this clinical course can be interpreted only as being, in a large measure, the result of pasteurized milk.

Raw cow's milk must not, on the other hand, be considered as having potent antiscorbutic properties. Its effect cannot be compared to the miraculous change which is brought about by giving orange-juice. This is especially striking when we take into consideration the small amount of orange-juice necessary to bring about a cure and compare it with the large amount of raw milk which is given. Raw milk, however, contains sufficient of the essential substances to prevent the development of scurvy.

It is possible that in addition to the pasteurization there are other factors in connection with the milk which enter into the causation of scurvy. Plantegna has laid emphasis on the freshness of the milk

5. Holst, A., and Froelich, T.: *Ztschr. f. Hyg. u. Infektionskrank.*, 1912, lxxii, 1.

both before and after pasteurization. This factor may be found to resolve itself into a question of reaction, of greater or less acidity, which experiments on animals have shown to be of importance. Against the justification of attributing scurvy to the heating of milk, the favorable statistics given by Variot and other French authors, including thousands of cases of infants fed on boiled milk, have always seemed conflicting evidence. Whatever may be the explanation of their results, it must be remembered that these statistics refer to patients treated in the dispensaries, and that they were not observed under ideal conditions. There can be no doubt that milk loses some of its antiscorbutic qualities as the result of heating; pasteurized to the degree which we are considering, 145 for thirty minutes, it seems to lose only a portion of its essential properties. The cases that developed in our wards on this diet were for the most part very mild. They showed petechial hemorrhages, some tenderness of the bones, a very slight degree of peridental hemorrhage, but they did not evince a tendency to progress. There seems to have been almost, but not quite, a balance between the demands of the body and the supply in the diet of the essential substances on which scurvy depends. They were not all, however, of this mild or immature type of case; two of the severest cases developed in infants receiving two-thirds pasteurized milk.

DIETETIC THERAPY

We have come to a consideration of dietetic treatment, which at once suggests the efficacy of orange-juice. Last year we gave, as routine, orange-juice that had been boiled for five or ten minutes and found that we were able to obtain satisfactory results. One ounce was given daily and, as far as we could judge, boiling did not lessen its therapeutic value. This year, for orange-juice we substituted the juice of orange-peel, which was prepared as follows:

The orange-peel was finely grated and 1 ounce of it was added to 2 ounces of water, a small amount of sugar being added to overcome the slightly bitter flavor. The juice of orange-peel seems to serve the same purpose as the juice of the orange itself. It is being used at the asylum at the present time, and after a trial of several months, we have come to the conclusion that it has marked antiscorbutic power. At first we made use of the peel to test its value, but have continued its use because it allows us to serve the oranges to the older children in the institution, and in this way is somewhat economical.

According to our experience, the efficacy of vegetables cannot be compared to that of orange-juice. Two cases of scurvy developed among the infants over one year whose diet included vegetables, mainly carrots. It is impossible to state how much vegetable the nurses gave

these two children; there is no reason to believe, however, that they received less than the twenty-eight other children in the ward. It is probable that they had a peculiar susceptibility to scurvy; one had exudative diathesis. When we reflect that sporadic cases of beriberi have been reported in which vegetables had been given that had been cooked for a long time, we must consider whether it is not possible that vegetables may also lose their antiscorbutic properties if cooked to a high degree. The experiments of Holst and Froelich⁵ would also seem to caution us in this regard; they found that the juice of white cabbage lost its antiscorbutic value when heated even to 60 C. for ten minutes.

One of the patients, an infant receiving malt soup, developed scurvy in spite of the fact that it was given a teaspoonful of cod-liver oil three times a day for one month before the disease manifested itself. It will also be noted that in the case of recurrent scurvy which we cited, the patient had been receiving cod-liver oil for some weeks previous to the onset of the second attack. Evidently this valuable therapeutic agent cannot be relied on as an antiscorbutic. This is of interest in view of the experiments of Osborne and Mendel⁶ showing the ability of cod-liver oil to promote growth in rats which had been stunted by means of a standard diet. Olive-oil certainly does not possess any antiscorbutic power. In the severest case of our group the patient had obtained a teaspoonful of olive-oil three times a day for a month before the development of scurvy.

The potency of potato was tried in some cases. It will be remembered that, in the scurvy of adults, the value of potato has been greatly lauded, and that epidemics of this disease have been reported to have followed a failure of the potato crop. First we made some trials with potato flour which is sold in the market; this was prepared with water and added to the milk in the same proportion as barley-water. It was soon evident, however, that potato flour cannot cure scurvy. We next employed mashed potato; a tablespoonful of boiled potato was added to a pint of water, using for this purpose the water in which the potato was boiled. In other words, instead of using a tablespoonful of barley to a pint of water, mashed potato was substituted. This was found very efficacious. The scorbutic symptoms quickly disappeared, although it did not seem to bring about the sudden change that is sometimes seen when orange-juice is given. It is probable that baked potato is just as valuable as an antiscorbutic.

In view of what has been outlined, at what age should we begin to give infants an antiscorbutic? There is no doubt that if an infant is fed solely on heated cow's milk the tissues begin to lose antiscorbutic substances — there is a negative balance of this material — from the

6. Osborne, T., and Mendel, L. B.: *Jour. Biol. Chem.*, 1914, xvii, 401.

very first days of life. Such being the case, it would seem that these essential substances should be supplied to the infant as soon as it is possible. As far as is known, there is no physiologic reason why orange-juice or potato should not be given in small quantities to an infant a few weeks of age. Two years ago, it was clearly shown⁷ by means of an examination of the duodenal contents, that starch-splitting ferments are present in the intestine of infants at birth, and are secreted in large measure after the first few weeks of life. It would also seem worthy of trial to substitute potato water for barley-water in the mixtures of pasteurized milk which are being distributed with such great benefit by the various diet kitchens in the larger cities. This will obviate the necessity of constantly admonishing the mothers not to omit orange-juice from the daily diet of their infants.

COMMENT

The chemical processes involved in scurvy are as yet unknown. There have been a few metabolism experiments connected with this disease, but they do not agree in their results. Lust and Klocman⁸ found a positive balance of mineral salts in the course of scurvy and a negative balance during convalescence. They describe a disturbance of elimination of the salts of the body, which is quite the opposite to what is found in rickets.

A more recent study of metabolism is that of Bahrt and Edelstein⁹ which is based, not on examinations during life, but on chemical analysis of the organs after death. These authors found a decrease of ash in the bones, especially of calcium and phosphorus very much as in rickets. A test of this nature, of the organs of the body, ought to afford reliable information. It should be noted, however, that in the case in question the patient had been under treatment for six weeks prior to death and that the tissues may therefore not have been in the active stage of the disease at the time of death. Further tests must decide which of these views is correct; from a clinical point of view, it is difficult to associate a marked deficiency of calcium salts with a disease in which fracture of the bones is a classical symptom, followed by a normal formation of callus. It should be emphasized that metabolic studies of this kind at present are necessarily incomplete, that after the various salts and organic substances are quantitatively analyzed, there is no doubt that more substances have been omitted than included in the chemical tests. This disease, furthermore, sharply emphasizes the fact that although an estimation of the caloric value

7. Hess, A. F.: The Pancreatic Ferments in Infants, *AM. JOUR. DIS. CHILD.*, October, 1912, p. 205.

8. Lust, F. and Klocman, L.: *Jahrb. f. Kinderh.*, 1912, lxxv, 663.

9. Bahrdt, H., and Edelstein, F.: *Ztschr. f. Kinderh.*, 1913, ix, 415.

of food is important, it may omit the very substances which are essential to health and life. In some of our cases the caloric value of the food was as high as 120 calories per kilo, body weight, but nevertheless there was a development of scurvy, accompanied by loss of weight and failure of nutrition.

In this connection we must mention the very interesting and suggestive studies of Funk.¹⁰ This author has coined the word "vitamines" for substances which are essential to the health and life of the body, and the lack of which produces a group of diseases which he has termed the "avitaminosen," including beriberi, scurvy, pellagra and rickets. The vitamins, Funk asserts, are crystallized nitrogen containing bodies of very complicated structure which are chemically defined, but concerning the exact structure of which we as yet know little. They are essential to life, although present in very small amounts. Such is the definition which Funk gives of the substances which he considers play an important and even vital part in nutrition.

Similar studies have been made by others, notably Stepp,¹¹ who terms these substances "lipoids," by which he means substances soluble in alcohol and in ether. He also found that animals could not live when deprived of these substances. Although these "vitamines" have not been satisfactorily isolated from a chemical point of view, and exception has therefore been taken to the term, there is no doubt from experiments on animals that these substances play an important rôle in the nutrition of the body. When they are removed from the diet the animals develop various nutritional disturbances, and regain their normal condition only when they are again added to the diet. These vitamins are thermolabile and are supposed to constitute a group of which there are various members. It is probable that one of this group is the vitamin which prevents the development of scurvy. It would also seem that this material is supplied in the mother's milk, and that this accounts for the fact that nursing infants do not develop scurvy.

SUMMARY

Infantile scurvy is a disorder characterized clinically by hemorrhage, for example, the classical bleeding into the gums and the subperiosteal hemorrhages of the long bones. A study of the cause of this bleeding, which must include a consideration of the clotting-power of the blood, forms the nucleus of this investigation.

For the coagulation tests blood was aspirated directly from the blood-vessels and oxalated. This plasma showed a slight diminution in clotting-power. This defect did not seem, however, to be the result of an insufficiency of calcium. The antithrombin was not increased.

10. Funk, C.: *Die Vitamine*, 1914, J. F. Bergmann, Wiesbaden.

11. Stepp, W.: *Deutsch. med. Wchnschr.*, 1914, No. 18, p. 892.

Small amounts of blood were also obtained by puncture of the finger. Examinations of this blood revealed a normal number of blood platelets. In other respects the picture was that of a simple secondary anemia, except that the hemoglobin was diminished out of proportion to the red blood-cells. A marked regeneration of these cells during convalescence, leading to a polycythemia, was also noticed.

These various departures from the norm are insufficient to account for the hemorrhages associated with the disease. The integrity of the blood-vessels was therefore investigated by means of a device which may be termed the "*capillary resistance test*." This test consists in subjecting the capillaries and vessels of the arm to increased intra-vascular pressure, by means of an ordinary blood-pressure band, and of observing whether this strain results in the escape of blood through the vessels—the appearance of petechial hemorrhages into the skin. The vessels of normal infants were found to withstand, without apparent disturbance, 90 degrees of pressure for three minutes, whereas the vessels of infants suffering from scurvy gave way under this pressure. The test is not specific for scurvy, but is a method of demonstrating a weakness of the vessel walls, whatsoever may be its cause.

In the course of an exceptional opportunity to observe scurvy in its incipency, numerous petechial hemorrhages of the skin or mucous membranes were frequently noted as one of the earliest signs of the disease; no sign, however, should be regarded as preeminently the primary symptom of scurvy.

It is generally recognized that scurvy has not only an exciting cause, but a predisposing cause. *The well-known "exudative diathesis" of Czerny was found definitely to predispose to the development of scurvy.* Whether there are other predisposing factors remains to be determined.

Several cases of scurvy developed in infants who were being fed on milk which was pasteurized to 145 F. for thirty minutes. They were cured by receiving fruit-juices or raw milk.

Orange-juice was found not to lose its efficacy as the result of being boiled for ten minutes. The juice of the peel was successfully substituted as an antiscorbutic for the juice of the orange.

Potato proved to be an excellent antiscorbutic. It is suggested that it be added to pasteurized milk as potato-water instead of the barley-water which is now commonly used as a diluent. In this way the necessity will be obviated of giving orange-juice.

Cod-liver oil or olive-oil, although given for weeks, did not prevent the development of scurvy.

16 West Eighty-Sixth Street.

INTERNAL HYDROCEPHALUS

AN EXPERIMENTAL, CLINICAL AND PATHOLOGICAL STUDY *

WALTER E. DANDY, M.D.

AND

KENNETH D. BLACKFAN, M.D.

BALTIMORE

Part 1.—Experimental Studies

1. INTRODUCTION

The term "hydrocephalus" is merely a symptomatic designation for an idiopathic disease. The subdivisions into acute and chronic, internal and external, congenital and acquired, are made according to no one standard, but according to several—pathological, clinical and embryological. Such subdivisions do not clarify the pathogenesis, but serve to obscure it. Chronic internal hydrocephalus, whether congenital or acquired, is the most important and frequent form encountered.

Internal hydrocephalus is characterized by a progressive accumulation of cerebrospinal fluid in the ventricles, causing their dilatation and a consequent cortical atrophy and, when possible, enlargement of the head. The disease is usually fatal; spontaneous recovery, however, does occur in a small percentage of cases.

Numerous forms of treatment have been suggested and tried, but, as the number of methods indicates, they have been almost uniformly unsuccessful. The etiology being so obscure, any treatment is necessarily empirical and consequently unsatisfactory. Successful therapy must depend on the identification and the treatment of the cause of the disease.

It is evident that internal hydrocephalus is due to an abnormality either in the formation or in the absorption of cerebrospinal fluid or possibly in both. Our studies—experimental and clinical—have been concerned with the development, the pathology and the diagnosis of internal hydrocephalus.

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* From the Departments of Surgery and Pediatrics of the Johns Hopkins University and Hospital. A preliminary communication of this study appeared in the *Journal of the American Medical Association*, 1913, lxi, 2216.

2. HISTORICAL

Reference to hydrocephalus is made by the earliest medical writers. Hippocrates is credited with suggesting surgical treatment by trephining the anterior part of the skull. He evidently thought that the accumulation of fluid was extracerebral.

Galen was the first to give special consideration to this disease, which played a conspicuous part in his theory of the "animal spirit." Galen was really advanced in his knowledge of the anatomy of the ventricles of the brain. He thought they were in free communication with one another and that they formed a closed system. He knew of the aqueduct of Sylvius and of the foramina of Monro. Galen, however, believed that the soul or "animal spirit" was contained in the ventricles and that here it underwent a process of purification; the purified products were supposed to pass into the pores of the brain and the waste products found their way through the pituitary body and were discharged into the nose as "pituita." He considered hydrocephalus due to some defect in this process of elaboration of the "animal spirit."

The teachings of Galen were accepted without question until Vesalius, in 1543, denied the existence of the "animal spirit." Following Vesalius a succession of distinguished anatomists have been interested in the study of hydrocephalus. Among them have been Willis, Sylvius, Rhazes, Celsus, Petit, Pacchionis, Brunner, Litré, Morgagni, Cotugno, Monro, Haller, Robert Whytt, and in the nineteenth century Magendie, John Hilton, Luschka and Key and Retzius.

Many theories regarding the content of the ventricles have been considered since the overthrow of Galen's theory of the "animal spirit." It has at various periods been regarded as water, air, vacuum, vapor, until finally it was proved to be a fluid. Verduc, about 1700, insisted that fluid was never present in the normal ventricles, and this agitation led to Haller's vapor theory. Haller had the advantage of a correct knowledge of the circulation of the blood and supposed the vapor to be exhaled by the arteries and inhaled by the veins.

Cotugno (1770) first proved the existence of the subarachnoid space and in addition found fluid in this space in living fishes and turtles, but was unable to demonstrate fluid in dogs because the spinal cord so closely filled the dural envelope. Though he was the real discoverer of the existence of cerebrospinal fluid in the living animal, his findings were not accepted because of the firm belief in Haller's vapor theory. At this time all fluid was explained on the basis of some pathological process or as a post-mortem condensation of the vapor.

Galen's teaching that the pituitary body was the portal of exit of the ventricular contents was held by many until the end of the eighteenth century. Haller denied this function to the pituitary body, but Petit (1718) and even *Monro* (1793) supposed that hydrocephalus was due to sclerosis of the pituitary body, which effectually closed the channels of exit from the ventricles.

Monro (1793), after whom the foramen of *Monro* is named, was also interested in the study of hydrocephalus. The presence of a foramen (the foramen of *Magendie*), leading from the fourth ventricle to the subarachnoid space as claimed by Haller and *Cotugno*, was denied by many, including *Monro*. He said:

The bottom of the fourth ventricle has no such communication with the cavity of the spinal marrow as Dr. Haller supposed, being completely shut off by its choroid plexus and pia mater. As further proof that the four ventricles communicate with each other and that they do not communicate with the cavity of the spinal marrow, I have observed in the bodies of every one of fifteen children who died from internal hydrocephalus that all the ventricles were distended; that on cutting into one of the lateral ventricles, all the ventricles were emptied, that in these cases, the passages above described were greatly enlarged, and that in none of them was water contained in the cavity of the spinal marrow or between its pia and the dura mater.

So near to the cause of hydrocephalus, in his zeal to prove a closed foramen, *Monro*, unfortunately, mistook it for the normal condition and left the discovery of the communication between the ventricles and the subarachnoid space to *Magendie*.

Without doubt, *Magendie's* contribution is the most important that has been made to the subject of hydrocephalus. He demonstrated by experiments on animals (1) that fluid normally fills the ventricles and the subarachnoid space; (2) that free communication exists between the ventricles and the subarachnoid space by means of a foramen which now bears his name; (3) that the central and spinal subarachnoid cavities form a single freely communicating space, and (4) that the aqueduct of *Sylvius* or the foramen of *Magendie* was obstructed in several cases of hydrocephalus.

Magendie, however, did not understand why hydrocephalus should result from an obstruction, for he thought the pia secreted the cerebrospinal fluid. He was led to believe that in some way the fluid could readily make its way upward through these membranous obstructions, but for some reason which he did not understand, its return was impeded and accumulation in the ventricles resulted.

The existence of cerebrospinal fluid has since been admitted, but the other observations of *Magendie* have been opposed. The controversy over *Magendie's* various claims and the views of more recent workers will be considered later.

3. INTERNAL HYDROCEPHALUS EXPERIMENTALLY PRODUCED

Flexner has noted that internal hydrocephalus sometimes follows the injection of the meningococcus into the subarachnoid space of monkeys. With this exception, we have been able to find no instance of hydrocephalus experimentally produced. The more common pathological processes producing internal hydrocephalus are usually so large (tumors) or so diffuse (inflammations) that it has been difficult to determine their exact part in the production of this disease. It is obvious that if hydrocephalus can be produced by experimental means, it will be possible to obtain definite information regarding its cause.

We conducted two series of experiments. In one, the aqueduct of Sylvius was occluded and in the other, the vein of Galen or the straight sinus or both were ligated. In each series the experiment was such that the function of either the aqueduct or of the vein was not disturbed.

I. EFFECT OF OCCLUSION OF THE AQUEDUCT OF SYLVIVS

In this series of experiments, in which an obstructing body was placed in the aqueduct of Sylvius, an internal hydrocephalus invariably resulted. It should be emphasized that the obstructing body was so placed *in* the aqueduct that the topographical relations were undisturbed and the lumen of the vein of Galen unaffected. The resulting hydrocephalus was therefore due solely to the mechanical occlusion of this channel. It is preferable to use a small obstructing body and depend on the formation of adhesions gradually to produce total occlusion. When this is done, practically no postoperative irritative effects result. A small pledget of cotton proved most efficient as the obstructing body.

These experiments were performed most successfully on dogs. Cats and monkeys were tried, but without success. When carefully done, the operative mortality in dogs was negligible. The animals at the time of operation were from 2 to 6 months of age. At this age the sutures of the skull are united so that the resulting hydrocephalus causes cerebral atrophy rather than enlargement of the head. Cerebral atrophy and cephalic enlargement are merely different expressions of the same underlying cause—increased intracranial pressure. Until the sutures are united, enlargement of the head is permitted by diastasis; after union the ventricular dilatation can be compensated only by cerebral atrophy and to a lesser degree by the displacement of external fluid and the absorption of bone.

The obstruction was placed in the aqueduct of Sylvius through a subcerebellar route as follows: Under ether anesthesia and strict surgical precautions, a bilateral, suboccipital decompression was made

through a posterior median incision. The defects in the bone and dura were made as large as possible to facilitate the subsequent procedure. The pia-arachnoid binding the cerebellum and the medulla was carefully cut on each side of the midline and an opening made corresponding to the foramen of Magendie, which is absent in the dog. The cerebellum and the roof of the fourth ventricle were raised by a small retractor. Through the artificial opening in the roof of the fourth ventricle a small pledget of cotton on the end of a graduated carrier was passed along the floor of the fourth ventricle into the aqueduct of Sylvius (Fig. 1). The pledget of cotton was deposited by withdrawal of

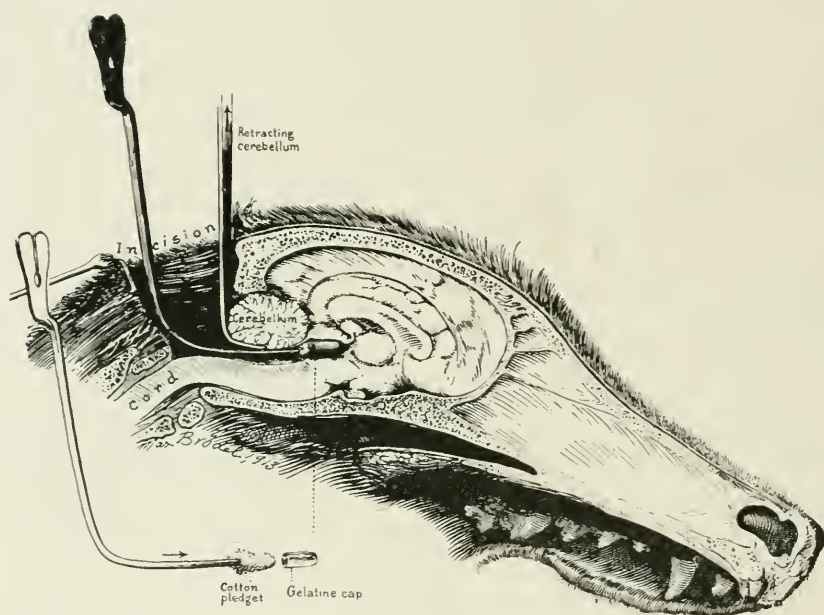


Fig. 1.—Midsagittal section of a dog's head to illustrate the method of procedure in the experimental production of internal hydrocephalus. The obstruction is placed in the aqueduct of Sylvius by the subcerebellar route.

the carrier. A refinement of technic, though of doubtful benefit, consisted in enclosing the cotton in a gelatin capsule immersed in liquid petrolatum. The cerebrospinal fluid dissolves the capsule surrounding the cotton (Fig. 2). The introduction of the cotton was rendered easier when it was enclosed. This, however, was not essential and was of questionable value, as adhesions form less readily about the cotton.

With care, an accurate deposition of the obstructing body can be obtained. The anterior tip of the fourth ventricle can be determined from the reading on the graduated carrier. Often additional evidence was afforded by resistance to the carrier's progress. It is very easy to

deviate slightly and force the instrument into the mesencephalon, naturally with destructive results on account of the immediate proximity of the pyramidal tracts and the nuclei of the upper cranial nerves.

The recovery following operation was uneventful. Frequently a slight spasticity, disturbance of equilibrium and weakness of the extra-ocular muscles persisted for several days following the operation, but all soon disappeared. Vomiting and lethargy, general pressure signs were evident from the time of operation and these were the principal manifestations of internal hydrocephalus. Doubtless a bilateral choked disk would have been present and given the best evidence of the onset

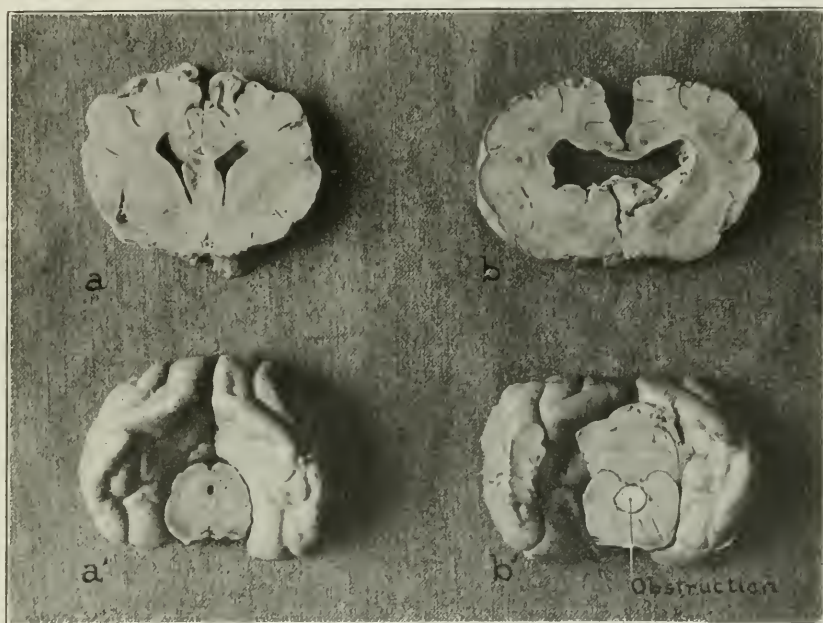


Fig. 2.—*a*, Cross-section of a normal brain of a dog at the level of the optic chiasm; *a'*, cross-section of the normal mid-brain of a dog to show the size of the aqueduct of Sylvius; *b*, cross-section of brain showing an experimental internal hydrocephalus of one month's duration; note the complete atrophy of the septum lucidum and fusion of the ventricles; *b'*, cross-section of the mid-brain of same animal showing the obstruction which had been placed in the aqueduct of Sylvius.

and progress of the intracranial pressure. Unfortunately, however, the eye-grounds were not examined. The animals were painlessly killed from three to eight weeks after operation. They were in good condition at the end of this time.

The citation of one experiment may be taken as representative of the entire group. Ether anesthesia was used in all experiments.

EXPERIMENT 1.—Jan. 9, 1911. Mongrel puppy, aged about 3 months; weight, $4\frac{1}{2}$ pounds.

Operation.—A small piece of unencapsulated cotton was passed into the aqueduct of Sylvius by the subcerebellar route described above—no operative complications.

Postoperative History.—January 11: Marked loss of equilibrium with tendency to fall backward. Slight dissociation of ocular movements; slight spasticity but no paralyses; frequent vomiting; marked lethargy. January 17: General condition good. Equilibrium normal. Walks around slowly but no tendency to playfulness; spasticity has disappeared, ocular movements normal, vomiting persists. January 28: Lies curled up in the cage most of time; takes no interest in surroundings. Sluggishly responds to stimuli; tendency to stupor. Ocular movements normal; vomiting more frequent. Losing weight. February 9: Killed by ether thirty days after operation.

Pathological Note.—During the removal of the calvarium the forceps punctured a greatly thinned cortex and entered a large, distended lateral ventricle. The intraventricular pressure was so great that cerebrospinal fluid spurted a distance of three feet. The accompanying photograph (Fig. 2 *b.*) shows the obstruction in the aqueduct of Sylvius well organized and apparently impermeable. The third and lateral ventricles were greatly dilated and the thickness of the cortex was correspondingly diminished. Only an occasional shred of septum lucidum remained. The vein of Galen was normal.

II. OCCLUSION OF THE AQUEDUCT OF SYLVIVS FOLLOWED BY EXTIRPATION OF THE CHOROID PLEXUSES OF BOTH LATERAL VENTRICLES

Though we removed the choroid plexus from one or both lateral ventricles in a series of experiments, the bilateral removal was followed by the insertion of an obstruction in the aqueduct of Sylvius in only one experiment. The object of this experiment was to see if extirpation of the choroid plexus modified the development of the internal hydrocephalus. The operative procedure was as follows: A bilateral, subtemporal decompression was made. On each side the dura was opened and a transcortical incision was carried into the lateral ventricle at the junction of the body and the descending horn. By dilating the cerebral opening with a nasal dilator, a good exposure of the entire lateral ventricle was obtained and the choroid plexus almost completely extirpated. Despite the great vascularity of the choroid plexus, bleeding was slight and was readily controlled by cotton pledgets.

At the same operation a suboccipital decompression was performed and an obstruction passed along the subcerebellar or transventricular route and deposited in the aqueduct of Sylvius. The choroid plexus of the third ventricle and probably remnants of the choroid plexus of the lateral ventricles still remained in front of the obstruction. Prevention of fluid accumulation was possible only to a modified degree. There was lethargy and occasional vomiting.

Thirty-five days after the first operation, the suboccipital wound was reopened and found in perfect condition. The cerebellum was herniated through the osseous defect made at the previous operation.

This showed an increased intracranial pressure. A fine pair of forceps was passed along the floor of the fourth ventricle and the obstructing body readily located and grasped. It was firmly in position; there was beginning organization, and some force was required to dislodge it. On its release there was a gush of cerebrospinal fluid. An internal hydrocephalus had resulted from the occlusion placed in the aqueduct

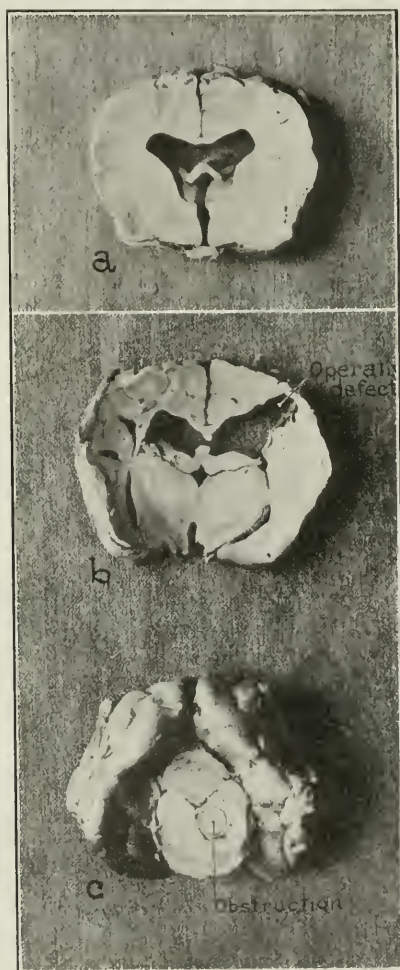


Fig. 3.—Cross-section of a brain of a dog showing an internal hydrocephalus of five weeks' duration which resulted from obstructing the aqueduct of Sylvius. The choroid plexuses of the two lateral ventricles were simultaneously extirpated: *a*, at level of optic chiasm; note atrophy of septum lucidum and dilated lateral ventricles; *b*, to show the operative defect in the cortex; the dilated ventricles are closed only by the meninges; the remains of the septum lucidum are still evident; *c*, midbrain showing the obstruction in the aqueduct of Sylvius.

of Sylvius thirty-five days previously, *in spite of the almost complete bilateral extirpation of the choroid plexuses of the lateral ventricles.*

The obstructing body was replaced at once in the aqueduct, the animal killed and the brain hardened *in situ* with formaldehyd solution. Subsequent examination showed a completely occluded aqueduct. The pia had healed, covering the operative wound in the cortex. The hydrocephalus was distinctly modified, being much less than a hydrocephalus of the same duration, in which the choroid plexuses had not been removed. The difference is well shown by comparing the ventricles (Fig. 3) in this specimen with the ventricles in Figure 2. The obstruction in each was of practically the same duration, and in both the occlusion of the aqueduct was complete. The contrast is less striking, however, than it should be, because the brain of the former animal (Fig. 3) was hardened *in situ* and the ventricles more nearly resembled their actual size, whereas the brain in the latter (Fig. 2) was hardened after removal, and the opening of the ventricles, before fixation, resulted in considerable shrinkage. The inference is to be made that the extirpation of the choroid plexuses modifies the degree of the internal hydrocephalus.

The preceding experiments prove that *an internal hydrocephalus results from a simple mechanical occlusion of the aqueduct of Sylvius. From this it is apparent that cerebrospinal fluid forms in the ventricles, at least more rapidly than it is removed, and that the aqueduct of Sylvius is necessary for its escape.*

III. LIGATION OF THE VENA GALENA MAGNA AND THE SINUS RECTUS

That internal hydrocephalus may be due to an obstruction of the great vein of Galen or of the straight sinus has been suggested. In most of the pathological specimens used to support this theory, tumors have been present in the corpora quadrigemina, the pineal gland, the cerebellum or in this immediate neighborhood, and compression of the aqueduct of Sylvius in all probability has also resulted. The most conclusive clinical proof is given in a few recorded instances of a thrombosis of the great vein of Galen or straight sinus. Newman (1882) reported a case of hydrocephalus in which a small thrombus was present in the vena Galena magna at its junction with the sinus rectus. Browning also presented a case with a small thrombus in the sinus rectus.

Internal hydrocephalus resulting from venous obstruction is dependent on the venous collateral circulation. A good description of the venous collateral circulation of the veins of Galen is given in Poirier and Charpy's "Anatomy," 1901, iii, 60. This work is based largely on

that of Browning, Hedon and Trolard. The internal cerebral system of veins, of which the great vein of Galen is the trunk, is largely independent of the external venous system. It is not, however, a completely closed system. Collateral circulation is definitely established with the external system by the basilar, superior cerebellar, internal occipital, temporal, posterior corpus collosal and several smaller tributaries of the vena Galena magna. This is demonstrated by the fact that colored solutions injected into the straight sinus pass to the external system by these channels. Poirier and Charpy, however, minimize the importance of this collateral circulation and think it is

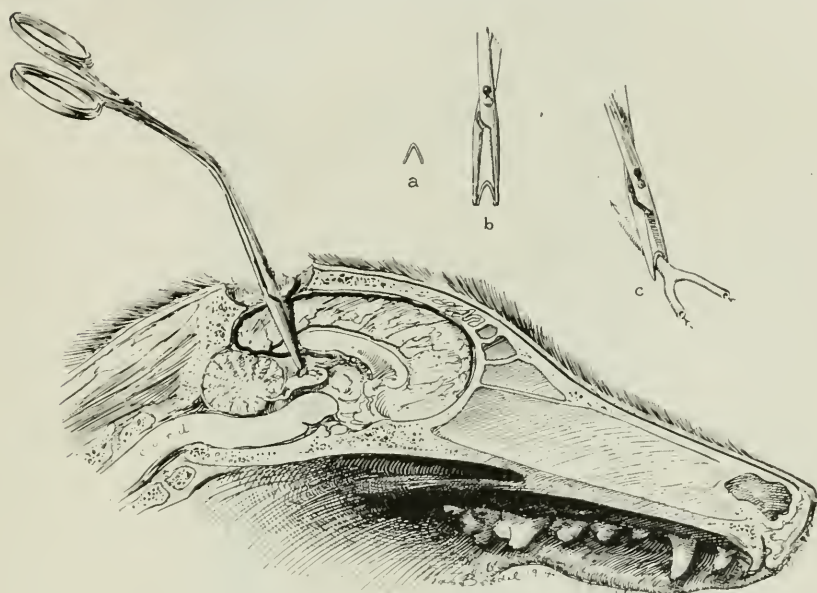


Fig. 4.—Drawing to indicate method of ligating the vena Galena magna. The silver clip is similar to that devised by Dr. Cushing. *a* shows the silver clip; *b*, in position in the clip holder, and *c*, its application on the vein.

insufficient to prevent internal hydrocephalus when the vein of Galen is obstructed. They further state that the small veins of Galen which drain practically the whole interior of the brain have almost no collateral circulation.

To determine the importance of venous obstruction in the production of internal hydrocephalus, we occluded the vein of Galen or the straight sinus or both in ten dogs. To do this a trephine opening was made just above the external occipital protuberance a little to either side of the midline. This opening was then enlarged with rongeur forceps. The dura was opened, reflected over the superior longitudinal

sinus and the occipital lobe separated from the falx cerebri. The straight sinus in the tentorium cerebelli (osseum) was traced downward to the vena Galena magna which is situated directly under the splenium of the corpus callosum. By careful blunt dissection the vein of Galen was isolated to permit the application of one or more silver clips (Fig. 4). These clips are similar to those designed by Dr. Cushing and act as most effective ligatures in wounds of such depth that ligation is impossible.

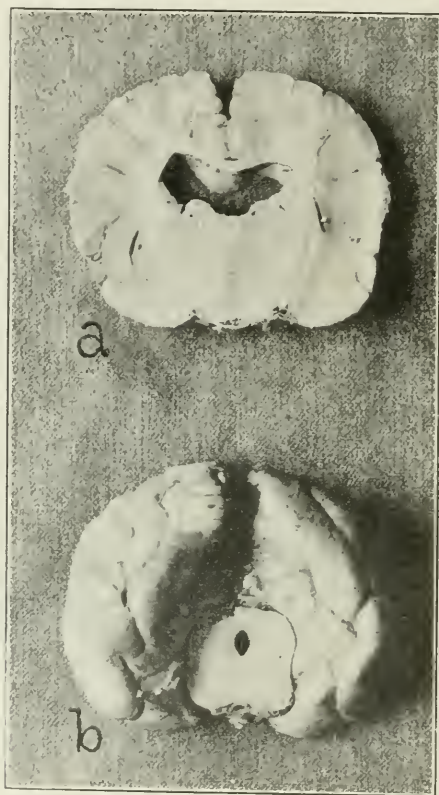


Fig. 5.—Internal hydrocephalus of three and one-half months' duration, produced by ligation of the vena Galena magna near its origin: *a*, dilated lateral ventricles, with atrophy of septum lucidum; *b*, to show the resultant dilated aqueduct of Sylvius; compare with normal Figure 2, *a*'.

In the ten dogs in which a ligation was thus accomplished, only one developed an internal hydrocephalus. In the other animals there was no evidence of ventricular enlargement.

Following the operation there was invariably an immediate recovery; in none were there any signs to indicate that the dogs were abnormal. All were as active and playful as the control animals. The

animals were under observation from one to eight months, and one gave birth to a litter of healthy puppies six months after the operation.

The single instance in which hydrocephalus resulted is of importance. The clip was placed just at the origin of the vena Galena magna, much lower than in any of the other experiments, thus barring the principal tributaries mentioned above from participation in the collateral circulation; the stasis resulting is no doubt similar to that in ascites which results from an obstruction to the vena cava, where the collateral circulation is insufficient to take over the additional work. The hydrocephalus was of three and one-half months' standing. The septum lucidum was largely destroyed, only shreds remaining. The ventricular dilatation was considerably less than in the dog in which the aqueduct of Sylvius was obstructed for thirty-five days and the choroid plexus of both lateral ventricles extirpated. The aqueduct of Sylvius was also larger than normal, showing the effects of its participation in the transmission of the increased ventricular fluid (Fig. 5).

In those dogs in which hydrocephalus did not develop, the clip was placed higher on the vein of Galen and nearer its junction with the sinus rectus. When the clip was so placed, or when the straight sinus alone was ligated, there was no evidence of fluid stasis and the ventricles remained normal in size, showing that below this point there was sufficient venous collateral circulation to prevent the formation of hydrocephalus.

It is therefore evident that a low obstruction of the vena Galena magna may result in the production of an internal hydrocephalus, but that a high ligation has no such effect.

4. THE FORMATION OF CEREBROSPINAL FLUID

I. THE EXISTENCE OF CEREBROSPINAL FLUID

Since the introduction of lumbar puncture by Quincke (1891), the existence of cerebrospinal fluid can be demonstrated at any time. That fluid rapidly reforms after withdrawal either from the ventricles or the subarachnoid space can also be demonstrated. Following ventricular puncture in hydrocephalus or after lumbar puncture in cerebral tumor with a postoperative cerebral hernia, the rapidity of the formation of fluid can be estimated. In either case the tension prior to the puncture is reestablished within a few hours, showing that the fluid removed by puncture has reformed during this time. The rapidity of formation can be observed in the rare condition known as rhinorrhea, in which the cerebrospinal fluid discharge may be 200 c.c. or even more in twenty-four hours.

The problem of the formation of cerebrospinal fluid concerns both the place and the manner of its formation.

II. THE PLACE OF FORMATION OF CEREBROSPINAL FLUID

Magendie thought cerebrospinal fluid was formed from the pia, saying:

The pia is almost exclusively a tissue of blood-vessels, and resembling very closely the pulmonary parenchyma, offers the most favorable conditions for a secretion, prompt and considerable. Everything, therefore, leads us to suppose the pia to be the secretory organ of the cerebrospinal fluid.

Magendie tried some injection experiments which tended to confirm this opinion, though he realized the necessity of further proof of a more direct character. He also realized the difficulty of harmonizing this view with his anatomical observations in hydrocephalus.

Lewandowsky was of the opinion that cerebrospinal fluid was a brain product and that only a small part of it could be ascribed to transudation from the choroid plexuses. Spina concurred with this view, but thought the cerebrospinal fluid was a product of transudation not only of the capillaries in the brain, but also in the pia mater. Schmorl noted serological differences in the cerebrospinal fluid of the ventricles and the subarachnoid space and concluded that fluid was formed both in the ventricles and in the pia. He further asserted that no communication existed between the ventricles and the subarachnoid space. Kafka, in a series of eighteen cases, was unable to verify these differences in serological (mainly Wassermann) tests.

The experiments concerning the production of internal hydrocephalus show that fluid forms in the ventricles. This is substantiated in hydrocephalus, in which there is obstruction to the outlets from the ventricles. The experiment in which a modified grade of hydrocephalus followed the total occlusion of the aqueduct of Sylvius and the bilateral extirpation of the major part of the choroid plexuses of the lateral ventricles is evidence of a direct character that the choroid plexuses, as has been suggested, are the organs from which this fluid is produced.

We do not maintain, however, that all cerebrospinal fluid is formed in the ventricles or from the choroid plexuses. Since transudation is partly responsible for this fluid formation, it is possible that fluid might be formed externally in the subarachnoid space, as has been suggested by Schmorl. Evidence for the extracerebral formation of cerebrospinal fluid is found in internal hydrocephalus, in which the foramina of Luschka and Magendie are occluded and all the choroid plexuses are enclosed in the ventricles. In such conditions though cerebrospinal fluid may be obtained by lumbar puncture it is always very small in amount and reforms very slowly. In Case 4, Group 1 (N. M.), never more than 3 c.c. were obtained, and frequently lumbar puncture yielded no fluid. In Case 5 of Group 1 (M. R.), all the

choroid plexuses were enclosed in the cerebral ventricles and the clinical and pathological observations showed an absence of communication between the ventricles and the subarachnoid space. By lumbar puncture, however, 5 c.c. of spinal fluid could be obtained. The ventricular and spinal fluids differed but little in composition. The amount of reducing substance (Fehling) was equal in the two. Hexamethylenamin, given by mouth, appeared in each in the same minute quantity, and the cell-count of the two fluids was the same. The choroid plexuses of this patient could obviously play no *direct* part in the formation of the fluid in the subarachnoid space. This fluid, small in amount, which reformed only after several hours, could be derived from one of two sources, either as a transudate from the pial vessels or as a transudate through the thin wall of the dilated fourth ventricle.

In Case 7, Group 1 (M. N.) the spinal and ventricular fluids were of similar composition, and an absence of communication between the ventricles and the subarachnoid space was clinically demonstrated. Twelve hours after a ventricular injection of phenolsulphonephthalein a minute trace of this color was present in the spinal fluid.

Since phenolsulphonephthalein, when present in concentration in the blood, does not appear in the cerebrospinal fluid, it is probable that the trace in the spinal fluid of this patient also was derived by transudation from the ventricles. The foregoing data are, however, insufficient to permit us to assert that the spinal fluid is formed in such a manner.

Although the choroid plexuses were known to Herophilus of Alexandria, Galen gave them the name by which they are known at the present day. Various functions have been ascribed to these structures. Willis (1664) thought they were blood-filters; Varoli, that they sucked up the ventricular fluid; Riolanus noted their exceptional vascularity and called them *rete morabile*; Nuck (1696) first believed them to be glands, a view which was soon received with favor, though various fanciful suggestions regarding them have been expressed since. Ruysch (1700) modified this general glandular conception to that of a cerebrospinal fluid-forming gland. Purkyne (1836) noted the epithelial character of their lining cells, but did not draw any conclusions concerning their function. Special attention was attracted to the secretory nature of this epithelium by Faivre (1854) and Luschka (1855).

Even at the present day there is no agreement of opinion as to the manner of production of cerebrospinal fluid.

One group favors the view that cerebrospinal fluid, like other body fluids, is produced by simple filtration through an animal membrane and that their differences depend on osmotic pressure between the capillaries and the serous spaces. This view is supported by Leonard Hill, Starling and Mestrezat. Another group, influenced by Heiden-

hain, chiefly, explains the formation of fluids on the basis of a cellular activity, or an active rather than a passive formation. In favor of this view are Galeotti, Cappellati, Cavazzani, Studnicka, Goldman, Schläpfer, Kingsbury, Mott and others.

1. The Manner of Formation, Based on the Composition of Cerebrospinal Fluid

Schmidt (1850) was the first to demonstrate differences between the composition of the cerebrospinal fluid and other serous fluids and between the blood-plasma and the cerebrospinal fluid. On this basis he suggested a secretory process of formation for cerebrospinal fluid. That which principally differentiates this fluid from other body fluids is its very low solid content and consequently its low protein content. The total solids are about one-seventh or one-eighth and the protein content about one three-hundredths of the blood-plasma content. This difference is most marked between the cerebrospinal fluid and the blood-plasma, but also obtains between the cerebrospinal fluid and the pericardial, peritoneal and other serous fluids. The specific gravity of the cerebrospinal fluid is 1.003, as compared to 1.028 for the blood-plasma. It is difficult, indeed, to understand how differences of osmotic pressure alone, acting on a common fluid medium and through the same vascular endothelium, could produce such differences as exist in the chemical composition of the various fluids.

As further evidence of the secretory theory of formation, it has been pointed out that the composition of cerebrospinal fluid resembles saliva more closely than it does the other serous fluids; while the salt content of saliva is somewhat higher, the water, total solids, protein content and specific gravity in cerebrospinal fluid are very similar. For some time a reducing body—pyrocatechin of Halliburton—was regarded as specific for cerebrospinal fluid. Halliburton has since shown this reducing substance to be glucose. Nawratzki confirmed the presence of sugar and estimated that it was present in about the same amount as in the blood. Cavazzani noted a minimum alkalinity of the cerebrospinal fluid as contrasted to the blood. He also declared that he had found a diastatic ferment, but Panzer and Lewandowsky were not able to confirm this finding. Kafka noted a lipolytic ferment. Other differences of a specific character have been reported, but most have been disputed, so that they are not now available as evidence of secretory activity.

Against the secretory theory of formation of cerebrospinal fluid is the mineral content of cerebrospinal fluid. Halliburton, Schmidt and Nawratzki determined that it was essentially the same as that of the parent blood-plasma and the other serous fluids. Simple filtration would seem to explain best this similarity of salt content.

2. *The Manner of Formation Based on the Anatomy and Histology of the Choroid Plexus*

The choroid plexuses are unique specialized structures, placed in every ventricle. That they are endowed with an exceptional blood-supply and covered by cells of a special character would seem to indicate that they are structures with a special function.

The elaborate blood-supply might well appear to indicate a filter-bed, while the specialized epithelium would indicate a gland. It would seem that there could be little doubt, from an anatomical point of view alone, that by one or both of these methods cerebrospinal fluid is supplied to the ventricles from the choroid plexuses. As noted above, Faivre and Luscka first emphasized the character of the epithelium and from analogy insisted on its secretory character. Their views have since been strengthened by the histological observations of Petit and Girard, Meek, Galeotti, Schläpfer, Goldmann, Imamura, Voshimura, Hworostuchin, Francini and others. The choroidal epithelial cells are large, cubical and often columnar, with a granular cytoplasm and basal nuclei. The cells are similar in appearance to gland cells, and such a histological picture is hardly conceivable without a secretory activity.

In addition to the general glandular appearance, granules, presumably of a secretory character, have been observed, both post-mortem and by intra-vitam staining methods. Galeotti (1897) first noted basophil and acidophil granules. These findings were substantiated by Bibergeil and Levaditi, Francini, Schläpfer and Goldmann, principally by the use of intra-vitam staining methods. Hworostuchin observed mitochondria, which he thought indicated the secretory activity of the plexuses. In addition, he noted the presence of nerves in the choroid plexus.

3. *The Manner of Formation Based on the Action of Drugs on the Rate of Production of Cerebrospinal Fluid*

It has been suggested that cerebrospinal fluid is formed by the secretory activity of the epithelium of the choroid plexus, because after the administration of drugs which stimulate glandular secretion there is supposed to be an increased production of cerebrospinal fluid and the cells show a histological change similar to the discharged appearance of the cells of the salivary glands. Petit and Girard, and Meek observed a swollen appearance of the choroid epithelium, a peripheral cytoplasmic clear zone and often cellular rupture following the administration of pilocarpin; Capelleti, Cavazzani and Petit and Girard obtained after the injection of pilocarpin an increased flow of cerebrospinal fluid from a subarachnoid fistula and compared this with

the effect on the salivary glands. They also noted an increase following ether, amyl nitrite and a diminished flow following atropin and hyoscyamin. Sicard was unable to confirm this. Dixon and Halliburton recently considered this subject in detail. They found only a slight increase of cerebrospinal fluid following injection of pilocarpin, atropin, amyl nitrite and various salts; and a definite increase following ether, chloral hydrate, chloroform, choroid plexus extract and brain extract.

In order that conclusions of value may be drawn from experiments of this nature, several precautions are necessary. The anesthetic must be constant and the animal must be sufficiently anesthetized to insure perfect quiet throughout the experiment. Vapor anesthetics cause great variations in the rate of flow of the fluid, and change of respiration produces similar results. To minimize these influences we used chlorbutanol, administered by stomach-tube; with this drug a very even anesthesia was secured. Rather than insert a cannula at random into the subarachnoid space, we exposed and trephined the atlas, and opened the dura by a stellate incision. Into the trephine opening in the atlas a special fitting cannula was inserted. The animal was then placed in a sling in such a manner that the cannula was at the most dependent part, and the fluid from both the head and the spinal canal ran into this as into a funnel. By this technic, bloody fluid was not obtained, and fluid did not accumulate as occurs when a needle is inserted through the dura. Clogging of the cannula does not occur and the experiments may be continued for several hours. To insure a steady outflow of cerebrospinal fluid we waited from fifteen to twenty minutes, or until the accumulated fluid had escaped. Drops were counted over arbitrary periods of five minutes. The results of these observations are represented in the accompanying charts (Fig. 6).

The most striking and uniform result obtained in these experiments followed the temporary compression of the jugular veins. Except in one instance there was always a marked and instantaneous increase of cerebrospinal fluid following jugular compression. We believe this can be explained only by an increased production of fluid. It is conceivable that it might be due to displacement of fluid by the cerebral congestion. If this were so, a retarded flow would be expected after the restoration of the equilibrium in the blood-vessels, but in each instance the previous level of fluid escape was reestablished. Moreover, the same results were obtained following jugular compressions frequently repeated at short intervals. When pressure on the jugular veins was maintained for a longer period of time, the increased flow did not continue, but gradually returned to normal. This was due, no doubt, to rapid establishment of collateral venous circulation.

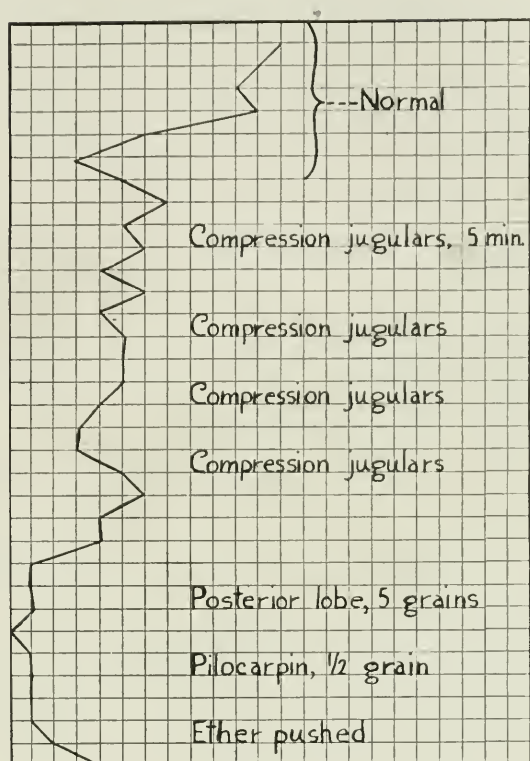


Figure 6 A.

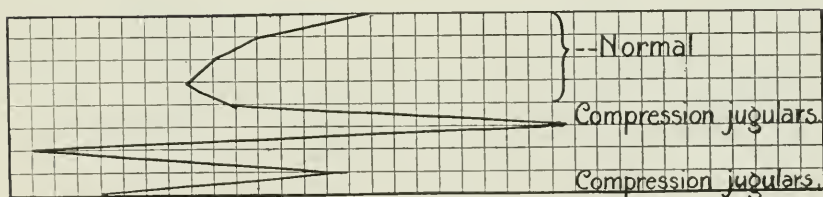


Figure 6 B.

Fig. 6.—Curves representing actual flow of cerebrospinal fluid from sub-arachnoid fistula, as influenced by drugs and mechanical factors. The base line represents time, each division being a five-minute interval. The vertical line represents the actual number of drops in each five-minute interval. The drugs used are entered during the progress of the curves.

(The remainder of these curves are shown on succeeding pages).

Since general cerebral venous stasis (jugular compression) results in increased cerebrospinal fluid formation, the place of formation of this fluid is probably from the vessels on the surface of the brain as well as in the ventricles. Owing to the efficient collateral on the surface of the brain, the formation of the fluid there is but transient, whereas in obstruction to the vein of Galen (low ligation and poor collateral) the increased production in the ventricles is continuous.

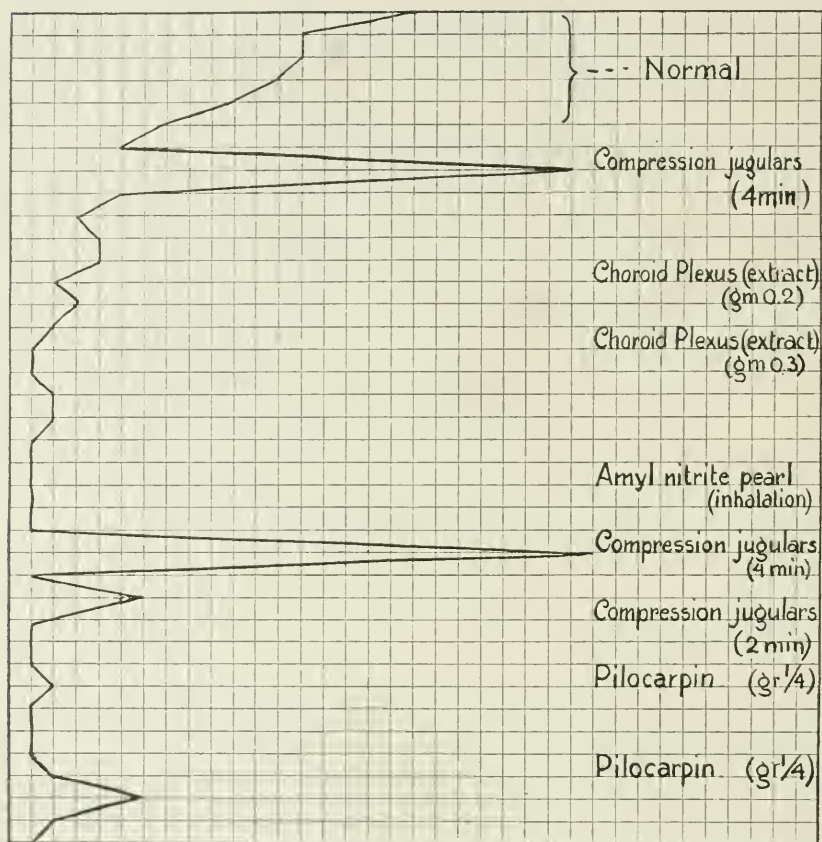


Figure 6 C.

In a number of experiments ether caused an increased production of fluid. It is probable that this increase is also due to venous stasis. The effect is not continuous, but occurs regularly with each application of ether. Amyl nitrite caused no such increase of fluid. The effect of pilocarpin on the increase of fluid production is slight, but always positive. When compared to the secretion which results from the stimulation of the salivary glands, however, it is practically negli-

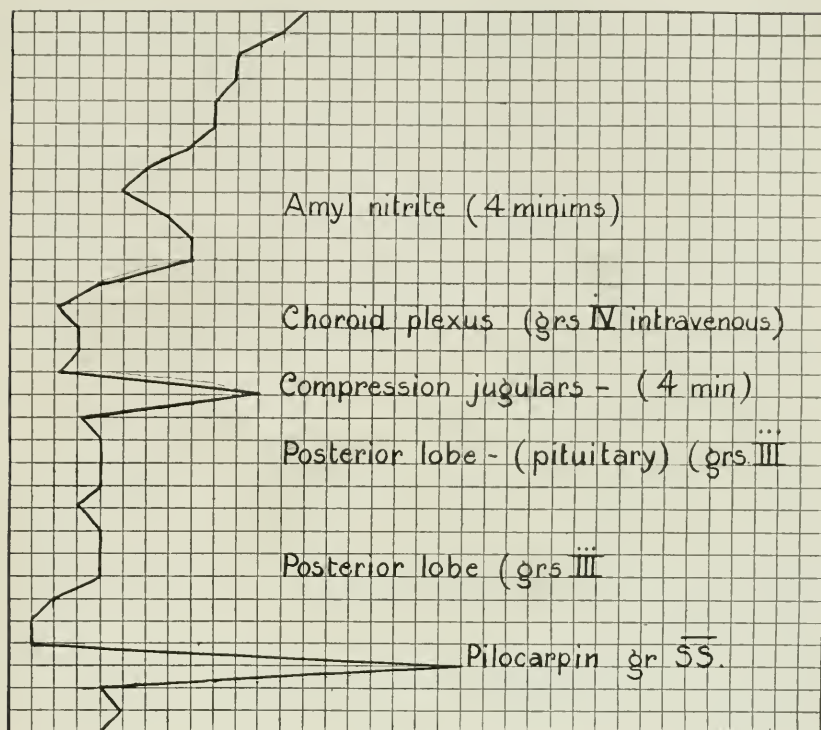


Figure 6 D.

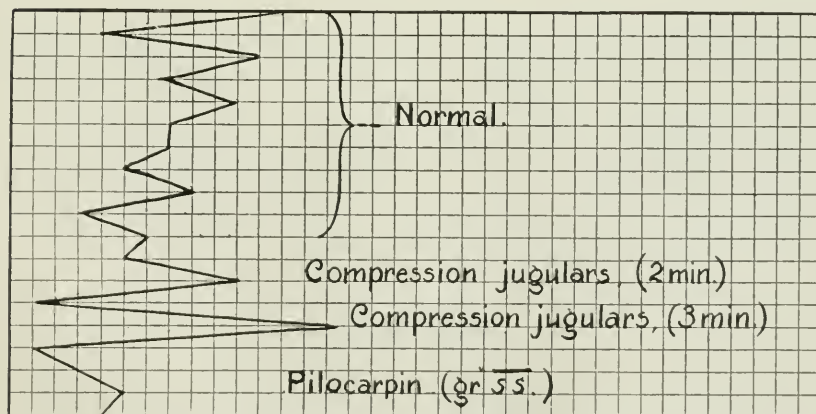


Figure 6 E.

gible. An animal when given pilocarpin will drown in its own salivary secretion, but the cerebrospinal fluid outflow increases only a few drops. We hesitate to make any positive deductions of glandular activity on such small though fairly constant results. Though no mechanical factors which might cause congestion and thereby filtration were noted during these experiments, this possibility must be borne in mind.

Repeated intravenous injections of freshly prepared aqueous extracts of choroid plexus and of posterior lobe of the pituitary body of the ox or sheep failed to produce an increased rate of flow of cerebrospinal fluid. This is contrary to the results of Dixon and Halliburton. They obtained a definite increase after the injection of extract of choroid plexus.

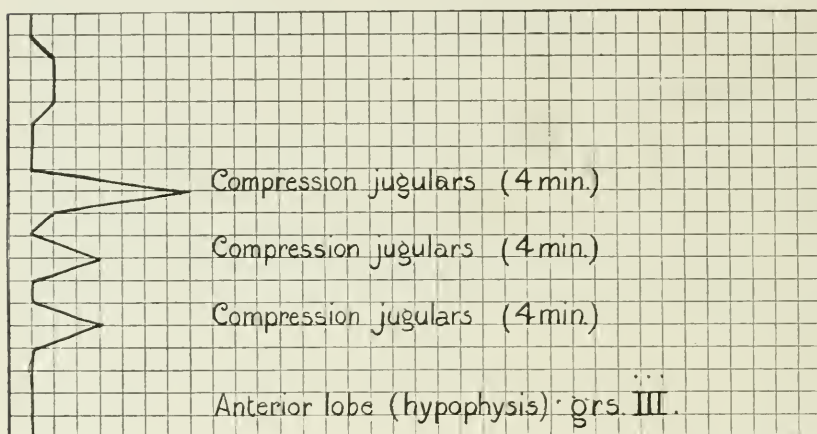


Figure 6 F.

Following the experiments with pilocarpin the choroid plexuses were removed for microscopic examination. We were unable to find definite histological alteration in the structure of the gland. Frequently, ruptured cells were observed, but these are often seen in the normal choroid plexus. From a purely objective point of view, it was impossible to tell from the choroid plexus whether or not a previous injection of pilocarpin had been made.

4. *The Manner of Formation Based on the Impermeability of the Choroid Plexus*

One of the strongest arguments in favor of the secretory theory of cerebrospinal fluid formation is the difficulty with which foreign substances pass from the blood to the cerebrospinal fluid. Were it entirely a simple mechanical process of filtration, it is difficult to under-

stand why simple substances should not readily pass through into the cerebrospinal fluid. It has been observed frequently that when very large doses of potassium iodid are administered, none passes into the cerebrospinal fluid. It has also been noted that in obstructive jaundice, bile pigments cannot be demonstrated in the cerebrospinal fluid. It is evident that a mechanism which can prevent the passage of certain substances into the cerebrospinal fluid must play a very important rôle in the prevention of the hematogenous transmission of infections to the central nervous system, and, for the same reason, when affections of the central nervous system exist, they are correspondingly refractory to remedies conveyed by the blood.

Such an impermeability to the cerebrospinal fluid has been shown to exist for numerous substances. Sicard was unable to obtain methylene-blue or potassium iodid in the cerebrospinal fluid when large doses were given subcutaneously, intravenously or by mouth. Rotky was unable to detect iodids, bromids, salicylates, mercury or bile pigments. These observations have been extended to include serological investigations. Widal and Sicard could not demonstrate agglutinins or immune bodies in the cerebrospinal fluid in typhoid fever. The behavior of the Wassermann reaction in the cerebrospinal fluid of hereditary syphilis without involvement of the central nervous system gives further evidence of the impermeability of the choroid plexus to foreign substances. In the majority of patients¹ whom we examined, the reaction was positive in the blood, but in no instance was there a positive reaction in the cerebrospinal fluid.

This impermeability, however, is not absolute; traces of many substances have been found in the cerebrospinal fluid. In certain diseases affecting the central nervous system there is a permeability. Sicard, Rotky, Capka and Mott showed this in meningitis, diabetes and uremia. Achard and Ribot observed traces of potassium iodid, Lewin and Bernard traces of salicylates, and Sicard traces of mercury in chronic mercurial poisoning, Olmer and Tian, Castaigne and others noted bile pigments in jaundice. Crowe noted hexamethylenamin, Rotky uranin and Lewandowsky strychnin. Zaloziecki observed immune bodies and agglutinins in typhoid fever, and thought that their quantity was dependent on the albumin content of the cerebrospinal fluid and the high concentration of immune bodies in the blood. We determined the presence or absence in the cerebrospinal fluid, of various substances after ingestion, and intravenous and subcutaneous administration. These observations were made on animals and in patients from the hospital wards. The results are given in Table 1.

1. These were patients from the Pediatric Clinic and the observations have not been published.

TABLE 1.—EXPERIMENTS TO DETERMINE THE PRESENCE OR ABSENCE OF VARIOUS SUBSTANCES IN THE CEREBROSPINAL FLUID AFTER ORAL, INTRAVENOUS AND SUBCUTANEOUS ADMINISTRATION

I. ANIMAL TESTS

Substance used	Amount	How given	Time of test after administration	Test in C. S. F.*	Other fluids
Methylene blue	30 c.c.	Intravenous	45 min.	—	Aqueous humor negative.
Indigocarmine	60 c.c.	Intravenous	30 min.	—	Peritoneal and pericardial positive; aqueous humor negative.
Phenolsulphone-phthalein	100 mg.	Subcutaneous	90 min.	—	Pericardial and aqueous humor negative.
Potassium iodid	30 gr.	Subcutaneous	60 min.	—	
Potassium iodid	60 gr.	Mouth	4 hrs.	—	None in aqueous humor.
Potassium iodid	50 gr.	Intravenous	30 min.	—	Pericardial fluid negative.
Strychnin	¼ gr.	Subcutaneous	15 min.	--	
Morphin..	½ gr.	Subcutaneous	30 min.	--	
Trypan blue	1 gm.	Intravenous	60 min.	—	
Hexamethylamin	45 gr.	Mouth	60 min.	+	Pericardial pleural fluids and aqueous humor positive.

II. CLINICAL TESTS

Hexamethylamin	10 gr.	Mouth	2 hrs.	+
Bile pigments	Obstruction 2 months	2 mos.	—
Bile pigments	Catarrhal jaundice 3 weeks	3 wks.	—
Bile pigments	Obstruction 3 weeks	3 wks.	+
Sodium salicylate	30 gr.	Mouth	60 min.	+
Potassium iodid	40 gr.	Mouth	40 min.	—

* In this column + means positive and — negative.

These results confirm those of many previous investigators. Of the various substances used, only hexamethylenamin and sodium salicylate were detected in the cerebrospinal fluid. The test for these substances is very delicate, and this may explain their detection in the cerebrospinal fluid. It is worthy of note that in dogs sodium salicylate and hexamethylenamin were obtained, in traces, in the vitreous humor. In several of the animal tests the aqueous humor was examined and the findings were almost identical with those of the cerebrospinal fluid.

It is striking that in spite of the actual flooding of the blood with colored solutions, such as phenolsulphonephthalein, indigocarmine, trypan blue and bile pigments, not even traces are present in the cerebrospinal fluid. In our experiments the animals were deeply colored following intra-vitam staining with trypan blue, and even the choroid plexuses were deeply stained, but the cerebrospinal fluid remained colorless—an observation frequently made by Goldmann. Indigocarmine was found in both the peritoneal and the pericardial fluids, but not in the cerebrospinal fluid or in the aqueous humor.

From these observations it would appear certain that the passage of substances into the normal cerebrospinal fluid is very difficult, and that when it occurs they appear only in faint traces. It is also apparent that there is greater difficulty in the passage of substances into the cerebrospinal fluid than into the other serous fluids. It seems difficult to attribute this fact to mechanical inhibition alone, but rather to a selective or discriminating cellular activity.²

IV. SUMMARY OF THE FORMATION OF CEREBROSPINAL FLUID

It can be definitely stated that cerebrospinal fluid forms in the ventricles. From evidence partly direct, but more largely indirect, there can be but little doubt that the choroid plexuses (possibly including the ependyma) produce this fluid. Whether this formation is alone by secretory or mechanical means or by both is impossible to say absolutely from the evidence at hand. Certainly fluid is readily and rapidly formed by the induction of venous stasis, and when the collateral circulation is insufficient (as the small veins of Galen and the beginning of the large vein of Galen), the increased production may be continuous and hydrocephalus result. How far the normal

2. Ducrot makes an interesting observation which, if substantiated, is indicative of therapeutic possibilities. He asserts that injections of methyl violet are followed by the appearance of the contents of the blood-plasma in the cerebrospinal fluid and in the proportions found in the blood. In jaundice, bile also readily passes into the cerebrospinal fluid following methyl violet injection. His explanation is that methyl violet paralyzes the secretory choroidal epithelium and the result is a temporarily inactive membrane. Filtration is then inhibited. This he also uses as proof of the secretory formation of cerebrospinal fluid. After several hours the effects of this drug wear away and the normal action of the choroid plexus is again restored.

differences of intravascular pressure cause transudation or production of cerebrospinal fluid cannot, however, be inferred by the production of artificial pressures. The similarity of the saline content of the blood and cerebrospinal fluid would seem to be undoubted evidence that filtration must be partially responsible for this fluid production.

On the other hand, the histological character of the choroid plexus epithelium, the radical difference in the chemical composition of the cerebrospinal fluid in comparison to the blood and other serous fluids and the protection of the cerebrospinal fluid from substances in the blood (impermeability) necessitate the assumption of a cellular or secretory activity. It therefore seems most probable that cerebrospinal fluid is formed both by filtration and by secretion.

5. *ABSORPTION OF CEREBROSPINAL FLUID*

The maintenance of a proper amount of cerebrospinal fluid in the ventricles and the subarachnoid space requires that there shall be an absorption equal to the formation. The first proof of an active circulation of cerebrospinal fluid was obtained by the experiments of Magendie. He demonstrated, after draining the subarachnoid space of as much fluid as possible, that there was such an active reformation that an equal amount of fluid could be again obtained on the following day or even sooner. He also demonstrated an active absorption of colored solutions when they were injected into the subarachnoid space and noted their presence in the jugular veins and in the urine.

Long before this absolute evidence, an active discharge of the ventricular content, whether fluid, vapor or animal spirits, had been presumed. As previously mentioned, Galen believed that the discharge of the material resulting from the purification of his animal spirits took place through the infundibulum and cribriform plate into the nose, where it was recognized as "pituita." Though Galen's theories of the animal spirits were attacked by Vesalius (1543) and later overthrown, his view that the infundibulum was the portal of exit for the ventricular content was accepted by many even until the time of Magendie (1825).

I. HISTORY

Lymphatics in the dura were described by Mascagni about 1775. Meckel (1777) supported this observation and referred to them as "vasa resortentia lymphatica." Arnold (1838) asserted the presence of lymphatics in the pia-arachnoid membranes and ascribed absorption of the cerebrospinal fluid to them. His (1850) and von Recklinghausen (1863) agreed with this observation and also noted the presence of perivascular lymphatics.

Böhme (1869) asserted the existence of a unique, independent system of valveless lymphatics which directly connected the subarachnoid

space with the pial vessels, forming in reality an accessory system to the blood-vessels. He maintained that there were large stomata which allowed free access to these vessels from the subarachnoid space. During congestion these vessels filled with blood, but despite the unguarded openings the blood did not pass into the cerebrospinal fluid. Milk and granular substances injected into the subarachnoid space, however, passed readily over into the veins through these stomata and the intermediary system of lymphatics. These stomata, demonstrable by silver nitrate staining, were similar to the diaphragmatic stomata, advocated only a short time before by von Recklinghausen.

Key and Retzius (1875) attributed the absorption of cerebrospinal fluid to the pacchionian granulations. During the injection of colored solutions under pressure into the subarachnoid space, they were able to observe such solutions passing through the pacchionian bodies into the longitudinal sinus.

II. METHODS OF TECHNIC

Though many investigations have been conducted to determine the method of exit of the cerebrospinal fluid, the results have been variable and inconclusive. They have been inconclusive chiefly because the experimenters have used artificial pressures, or the injections have been made post mortem. In all experiments here submitted the conditions have been as near normal as possible; no pressure was used, and the animals were alive (ether anesthesia). The results of the experiments represent as nearly as can be determined the natural processes of absorption.

The principal method used in solving this problem was by substituting inert colored fluids for an equal amount of cerebrospinal fluid and then determining the quantitative output of these substances in the urine. The substance must necessarily be one that is readily absorbed and quickly eliminated by the kidney.

We tried indigocarmin, methylene-blue and phenolsulphonephthalein. Methylene-blue and indigo-carmin were of little value in these experiments, so almost sole reliance was placed on phenolsulphonephthalein. Methylene-blue was but slowly excreted and appeared in the urine as a leuko-body, which rendered its quantitative estimation uncertain. Indigocarmin appeared more rapidly in the urine, but its color was affected by urinary pigments to such an extent that even an approximate quantitative value could not be estimated. Phenolsulphonephthalein met all requirements. The question of the excretion of phenolsulphonephthalein by the kidney has been investigated thoroughly by Rowntree and Geraghty, who introduced it as a test of the renal function. By virtue of its stability, its inert character, its rapid,

uniform and almost complete elimination by the kidney, its easy and accurate quantitative estimation, phenolsulphonephthalein is well adapted for this study. It has been used recently by Dandy and Rowntree in the estimation of absorption of fluids from the pleural and peritoneal cavities.

On account of the difficulty and uncertainty of performing lumbar punctures on dogs, owing to the great length of the cord, we obtained the cerebrospinal fluid from the cisterna magna. After exposing the occipito-atlantal membrane it was possible to puncture the transparent arachnoid membrane and siphon off the desired amount of fluid. The fluid was replaced by an equal amount of phenolsulphonephthalein solution at body temperature. One c.c. (6 mg.) of phenolsulphonephthalein was chosen as the amount for injection in these experiments. In each instance the time of the appearance of the substance in the urine and the quantitative output in the urine over periods of one and two hours were determined. The quantity excreted in the urine was determined by colorimetric readings in Rowntree and Geraghty's modification of the Autenrieth-Königsberger colorimeter.

It should be emphasized that these percentages should not be taken as absolute, for the total amount of phenolsulphonephthalein injected cannot be recovered in the urine. In the peritoneal and pleural cavities one can recover from 80 to 90 per cent., but, for some reason which is not evident, only 60 to 90 per cent. can be recovered after injection into the subarachnoid space. The results are sufficiently accurate for all practical purposes. The accompanying figures represent the percentage recovered of the amount injected.

III. THE RATE OF ABSORPTION OF CEREBROSPINAL FLUID IN DOGS

The following experiment is characteristic of the series:

EXPERIMENT 2.—May 26, 1911. Female dog, weight, 14½ pounds. One c.c. (or 6 mg.) of phenolsulphonephthalein substituted for 1 c.c. of cerebrospinal fluid (ether anesthesia). Time of injection, 10:02 a. m. Time of first appearance in urine, 10:07 a. m., five minutes. The hourly output is given in Table 2.

TABLE 2.—PHENOLSULPHONEPHTHALEIN EXCRETION IN EXPERIMENT 2.

Hours After Injection.	Time	Output of Phenolsulphonephthalein. Per Cent.
1	11:07 a. m.	16.6
2	12:07 a. m.	17.8
3	1:07 p. m.	13.6
4	2:07 p. m.	7.2
5	3:07 p. m.	4.5
6	4:07 p. m.	2.2
7	5:07 p. m.	1.3
8	6:07 p. m.	.3
9	7:07 p. m.	+

Total amount excreted in 9 hours..... 63.5

Five days later another injection on the same animal gave identical results.

We can conclude that there is an active circulation of cerebrospinal fluid. For a period of from three to four hours the absorption is fairly regular and after this time progressively diminishes. This diminution is in all probability due to the dilution by the fluid which is being constantly formed. It may be said that the cerebrospinal fluid is completely absorbed and renewed at least every four or six hours, or at least from four to six times every twenty-four hours. Experiments in which methylene-blue and indigocarmin were used were similar in time of appearance and disappearance, though a quantitative value could not be obtained.

The quantitative results of absorption from the human subarachnoid space are similar to these results in animals.

IV. DOES ABSORPTION OF CEREBROSPINAL FLUID TAKE PLACE INTO THE BLOOD OR INTO THE LYMPH?

There are two ways by which absorption of cerebrospinal fluid could occur—the blood and the lymph. Mott, who is the strongest exponent of the theory of lymphatic absorption, thinks perivascular lymphatics perform this function. The prevalent view, however, is that, with the possible exception of lymphatic connections along the olfactory and optic nerves, the central nervous system, including the meninges, is destitute of lymphatics. The present conception of the lymphatic system is that it is everywhere closed by endothelial cells, and that all its branches converge either to the thoracic or to the right lymphatic duct. Except for the work of Key and Retzius, who believe that the filling of the lymphatics occurs along the nerve sheaths, we know of no evidence of lymphatic absorption. Their experimental injections, however, were made under high pressure and were performed post mortem. Evidence of this character is open to the most severe criticism. Normally the cerebrospinal fluid does not pass along the sheaths of the nerves with exception of the olfactory and optic nerves.

Hill showed that when a colored solution was injected into the subarachnoid space it appeared in the urine in from ten to twenty minutes, but that the cervical lymph-glands were only slightly tinged after one or two hours. He concluded that absorption was directly into the blood.

We performed a series of experiments to determine the manner of absorption of cerebrospinal fluid. A cannula was placed in the thoracic duct and phenolsulphonephthalein was substituted for cerebrospinal fluid. The total lymph was collected, and the output of phenolsulphonephthalein in the urine was estimated.

EXPERIMENT 3.—April 18, 1911. Thoracic duct fistula. Ether anesthesia. The substitution of 1 c.c. (6 mg.) phenolsulphonephthalein for 1 c.c. cerebrospinal fluid (through the occipito-atlantal membrane). Catheterization of bladder.

Time of injection, 12:03 p. m.; first appearance in urine, 12:09—six minutes; first appearance in lymph, 1:45—one hour, thirty-six minutes.

Excretion of phenolsulphonephthalein in urine: First hour, 1:09 p. m.—9.5 per cent.; second hour, 2:09—12.2 per cent.

From this experiment it is evident that the cerebrospinal fluid is excreted in the urine long before it appears in the lymph, and that in two hours over 21 per cent. (even with an anesthetic) is excreted in the urine, while only a bare trace is present in the lymph. Presumably absorption took place directly into the blood. Proof of this is supplied by experiments, of which the following is an example:

EXPERIMENT 4.—April 30, 1913. Thoracic duct fistula. Chlorbutanol anesthesia. *Specimens of blood* taken from the carotid artery. Substitution 1 c.c. (30 mg.) phenolsulphonephthalein for 1 c.c. cerebrospinal fluid, through the occipito-atlantal membrane.

Time of injection, 3:30 p. m. The results are given in Table 3.

TABLE 3.—RESULTS IN EXPERIMENT 4

Time	Blood Examination	Lymph Examination
3:32 p. m.	0	0
3:33 p. m.	+	0
3:36 p. m.	+	0
3:58 p. m.	+	0
4:15 p. m.	+	0

Animal killed with ether.

Absorption took place directly into the blood and was very rapid. The dye was detected in specimens of arterial blood in three minutes, whereas there was no trace in the lymph after forty-five minutes. In one experiment of a similar nature a trace was found in the lymph in eighteen minutes after injection. In no case was there more than a trace even at the end of two hours—a striking contrast to the content in the blood and urine. The trace of color in the lymph appearing after a considerable interval might readily be derived from the blood.

It may be objected that absorption had taken place through the tributaries of the right lymphatic duct. For this reason the following experiment was performed:

EXPERIMENT 5.—May 10, 1911. Ether anesthesia. Thoracic duct fistula; dorsal laminectomy, the spinal cord and dura ligated at level of fifth dorsal vertebra. As a further precaution a second ligation was made 2 cm. above the first. Injection of 1 c.c. (30 mg.) phenolsulphonephthalein into the subarachnoid space of the segment distal to both ligations. Time of injection, 2:06 p. m.

Blood examination, 2:12 p. m., +; 2:20 p. m., +.

Lymph examination, 2:12 p. m., 0; 2:20 p. m., 0.

Animal killed with anesthetic.

It is therefore evident from these experiments that the lymphatics play no part in the absorption of the cerebrospinal fluid, but that absorption takes place directly into the blood.

V. ABSORPTION IS A DIFFUSE PROCESS INVOLVING THE ENTIRE SUBARACHNOID SPACE

The preceding experiment shows that absorption takes place also from the spinal subarachnoid space. When phenolsulphonephthalein is injected into the cisterna magna it is, as will be shown subsequently, distributed to all parts of the cerebral and spinal subarachnoid space in a very short time. It is believed by some that absorption is limited to the superior longitudinal and the other venous sinuses, and that the remaining cerebral and spinal vessels take no part in this absorption. In order to determine the part of the spinal subarachnoid space in the absorption of cerebrospinal fluid, experiments like the following were done:

EXPERIMENT 6.—June 2, 1911. Dorsal laminectomy; chlorbutanol anesthesia; ligation of dura and cord at the level of the fourth thoracic vertebra. A second ligature was placed 2.5 cm. above the first, to prevent absolutely the direct transmission of fluid from the lower segment into the cranial subarachnoid space. Fluid withdrawn from distal spinal segment and substitution of 1 c.c. (12 mg.) phenolsulphonephthalein. Animal killed with anesthesia.

Time of injection, 12:47 p. m.; time of appearance in urine, 12:53 p. m.—six minutes; 18.2 per cent. was excreted the first hour and 10.4 per cent. the second hour.

EXPERIMENT 7.—Similar to Experiment 6. June 8, 1911.

Time of injection, 2:32 p. m.; time of appearance in urine, 2:38 p. m.—six minutes; 15.1 per cent was excreted the first hour and 13.2 per cent. the second hour.

Animal killed with anesthesia.

It will be seen that there is a very high absorption from the spinal subarachnoid space; in fact, the amount of phenolsulphonephthalein excreted is nearly as much as from the entire subarachnoid space. There is, however, with such experiments an increase in pressure which cannot be prevented. The spinal subarachnoid space in the dog contains comparatively little fluid, so closely do the arachnoid and dura envelop the spinal cord. For this reason it is impossible accurately to substitute the amount of fluid which is withdrawn. The injection is consequently under tension, which must alter the rate of absorption and probably accounts for the rapid excretion. This permits the deduction that an active and rapid absorption takes place from the spinal subarachnoid space. Absorption is, therefore, a diffuse process. It takes place from the entire subarachnoid space and is not restricted to any particular portion of this space. Our results, therefore, show that the absorption of cerebrospinal fluid is directly into the capillary network of the entire subarachnoid space.

VI. THE EVIDENCE AGAINST THE ABSORPTION BY MEANS OF STOMATA

The principal exponents of the theory of stomata as a means for the absorption of cerebrospinal fluid are Böhm, Adamkiewicz, Reiner and Schnitzler. The strongest argument in favor of stomata is that granules have been observed to pass from the subarachnoid space into the veins. This can readily be shown in embryos, and with much greater difficulty in adults; but as mentioned above, and as shown by Mall, this is entirely dependent on pressure and the consequent tearing or rupturing of delicate tissues.

Stomata in the subarachnoid space were originally suggested by Böhm (1869), but his observations lack confirmation. Stomata in lymphatics of the central tendon of the diaphragm, as described by von Recklinghausen, have been proved to be artefacts. That there are stomata in blood-vessels is even more difficult to believe. If there were stomata in the blood-vessels in the subarachnoid space one would expect to find bloody cerebrospinal fluid as the result of venous congestion. The absence of blood cannot be explained by valves, as these have never been demonstrated.

In our experiments, India ink and lampblack *granules in suspension were substituted for an equal amount of cerebrospinal fluid*, and the animals used were kept under anesthesia for varying periods of time. Even after two or three hours there was no evident egress of granules. Specimens of blood from superior longitudinal sinus were examined microscopically at frequent intervals for granules, but with uniformly negative results. At the end of one, two or three hours there was a perfectly uniform distribution of granules throughout the entire cerebral and spinal subarachnoid space. There was no evidence of an accumulation in any particular locality. A number of the animals were frozen, and subsequently placed in formaldehyd solution; the sinuses were later opened, examined by sections and the blood in the sinuses also examined. Granules were present in the pacchionian granulations and along the walls of the longitudinal and other sinuses, but there was no suggestion of any passage into the lumen of the sinus. In each case the granules were separated by the arachnoid membrane and a layer of dura.

The blood in the sinuses was also free from granules. That granules of this size never pass out of the subarachnoid space is not maintained. In all probability there is an elimination by some vital activity, but evidently not by a free transit through preformed openings.

Further evidence of the absence of stomata is offered by a number of experiments in which pressure was used. If granules are injected into the subarachnoid space of adult dogs under a pressure of 100 mm.

of mercury or less there is no passage of the granules into the venous sinuses. These high pressures kill the animal. The longitudinal and lateral sinuses can then be exposed for their entire distance, but even after the lapse of an hour or even longer granules are not found in the sinuses. The pacchionian granulations are full of granules, but there is no passage through their walls. It is evident, therefore, that with the animals' own processes of absorption during life and even with highly artificial pressures after death, no evidence can be obtained of a passage of granules, by way of stomata, either into the sinuses or into any other part of the vascular system.

It has been shown in the foregoing experiments that absorption is by a general or diffuse process involving the capillaries in the entire subarachnoid space. Since the absorption from the spinal subarachnoid is *at least proportionally as great* as from the entire subarachnoid space, it is not necessary to attempt to explain the absorption of cerebrospinal fluid by means of stomata along the cerebral venous sinuses.

VII. THE EVIDENCE AGAINST THE ABSORPTION OF CEREBROSPINAL FLUID BY THE PACCHIONIAN GRANULATIONS

The theory that the pacchionian granulations play a part in the absorption of cerebrospinal fluid is due to the work of Key and Retzius. This view has received much support. The pacchionian granulations are really arachnoid diverticula which project into the lumen of the sinuses and into the bones of the vault of the skull. They are lined by a layer of arachnoid with a superimposed layer of dura, which is a far greater mechanical impediment to the passage of fluid than the simple endothelium lining of the capillaries in the pia arachnoid. The pacchionian granulations, moreover, are not present at birth or are developed so poorly as to escape notice. They increase in size and number with age and with intracranial pressure. It is asserted that in many animals they are absent.

Any evidence of the passage of fluid through the pacchionian granulations during life would be very difficult, if not impossible to obtain. Consequently, all proof is dependent on post-mortem injections. In such a condition it is possible to force fluid through the pacchionian granulations into the sinuses with very high pressure. Under a still higher pressure it is even possible to force water from the subarachnoid space into the nasal cavity.

The best evidence against the absorption of cerebrospinal fluid through the pacchionian granulations is the general character of the absorption from the subarachnoid space.

VIII. COMPARISON OF ABSORPTION OF CEREBROSPINAL, PERITONEAL AND PLEURAL FLUIDS

The absorption of fluids from the peritoneal and pleural cavities has been studied by Dandy and Rowntree. They showed that absorption of fluids from these spaces was a diffuse process, and was not dependent on the posture assumed. It was also demonstrated that absorption was directly into the blood and that lymphatics played no part. The absorption from these cavities is much more rapid than from the subarachnoid space. A comparison between the absorption

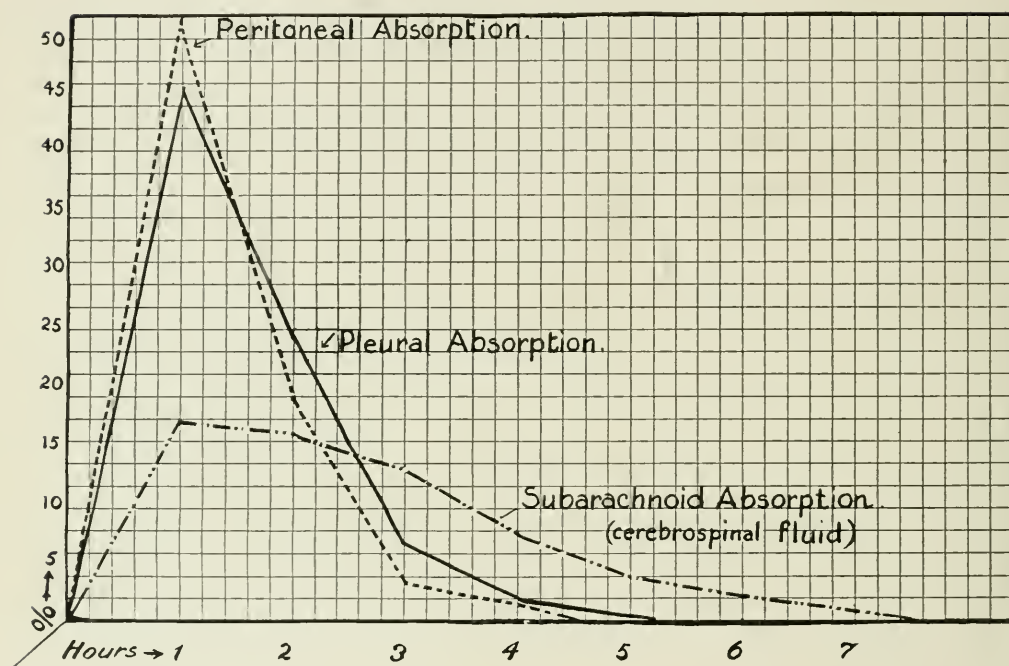


Fig. 7.—Curves to compare the total excretion of peritoneal, pleural and cerebrospinal fluids. The base line represents time divided into one-hour intervals. The vertical line represents absorption (percentage of excretion) of phenolsulphonephthalein in the urine.

of fluid from the pleural and peritoneal cavities with that from the subarachnoid space is shown in the accompanying chart. The time of first appearance of phenolsulphonephthalein in the urine was practically the same in all. The output from the pleural and the peritoneal cavities was more rapid than that from the subarachnoid space (Fig. 7).

IX. ABSORPTION FROM THE VENTRICLES

In order to complete the discussion of the absorption of cerebrospinal fluid it is necessary to consider briefly here some of the clinical observations, the details of which are given in a subsequent part of this article. In seven cases of hydrocephalus the communication between the ventricles and the subarachnoid space was found to be totally obstructed. An excellent opportunity to estimate absorption from the ventricles was thus allowed. When phenolsulphonephthalein was introduced into the ventricles of these patients its first appearance in the urine was greatly delayed (thirty or forty minutes or longer) and never was there an elimination of more than 1 per cent. during the two hours following the first appearance in the urine. This was irrespective of the dilatation of the ventricles or the quality of fluid present.³

The excretion of phenolsulphonephthalein after such an injection continued ten days and even longer. The dye was present in the ventricles also for the same length of time. It is evident, therefore, that practically *no absorption takes place from the ventricles*.

6. COMMUNICATION BETWEEN THE VENTRICLES AND THE SUBARACHNOID SPACE

The preceding experiments show that fluid forms in the ventricles and that it is absorbed from the entire subarachnoid space. It is evident that the normal balance between the production and the absorption of cerebrospinal fluid depends on an adequate communication between the place of formation and the place of absorption, namely, between the ventricles and the subarachnoid space.

Six foramina of communication between the ventricles and the subarachnoid space have been described. The foramen or canal of Bichat was first described (1819) as a median opening accompanying the vena Galena magna and affording communication between the third ventricle and the subarachnoid space. Soon afterward, Bichat added a foramen at the tip of each lateral ventricle—the lateral foramina of Bichat. Magendie, Luschka, and Key and Retzius proved these three foramina to be artefacts, as they were evident only after pressure was used. Mierzejewsky and Merkel (1872) again asserted the existence of a foramen from the tip of each lateral ventricle. Though regarded by most anatomists as artefacts, they are still believed by many to exist.

3. That tension of the intraventricular fluid has no effect on the absorption from the ventricles is shown by the fact that before and after the removal of 90 c.c. of ventricular fluid in Case 4, N. M., Group 1, the absorption was exactly the same (0.25 per cent. in two hours).

Though a communicating foramen at the fourth ventricle was suspected by Cotugno and others, its existence was first demonstrated by Magendie in 1825. Renault (1829) proved that no such foramen existed in the horse and that hydrocephalus in this animal did not result from its absence. Magendie confirmed the findings of Renault, though he continued to maintain the importance of this foramen in man. Krause (1843) maintained that all the ventricles, including the fourth, were sealed by pia, and that the foramen of Magendie was an artefact produced either by pressure or by dissection. Todd (1847) and Reichert (1861) expressed similar views. Virchow (1854) strongly opposed the theory of the existence of the foramina and of any communication between the ventricles and the subarachnoid space or between the cerebral and the spinal subarachnoid spaces. "There is no direct communication between the subarachnoid spaces, either between each other or with the cavities of the brain, and the fluid contained in them cannot thus simply rise or fall."⁴ The weight of his teachings was sufficient to retard greatly the acceptance of Magendie's views.

The existence of the foramen of Magendie was, however, supported by capable anatomists. Luschka (1854) verified the absence of this foramen in the horse and thought that the absence of hydrocephalus was explained by the lateral foramina which he described. These foramina are present in all animals and are larger in those in which there is no central foramen. He unquestionably substantiated the existence of the central foramen and named it in honor of Magendie. Key and Retzius (1875) confirmed the findings of Magendie and Luschka in every particular.

Retzius in 1896 examined one hundred brains and found the foramen of Magendie absent in two and the foramina of Luschka absent in three. This was confirmed by Hess and Cruveilhier. Cannieu (1898), however, after numerous injections and histological studies, concluded that the evidence in favor of communication could be explained by artefacts and that the ventricles formed a closed system everywhere lined by ependyma. Testut also believed this. Schmorl expressed a similar view after noting serological differences between the fluid in the ventricles and the subarachnoid space. He believed that this not only denoted a double origin of cerebrospinal fluid, but that the absence of the foramina of Magendie and Luschka was to be deduced therefrom.

4. "Die subarachnoidealen Räume stehen in keiner offenen Verbindung, weder unter sich, noch mit den Hirnhöhlen, und die in ihnen enthaltene Flüssigkeit könne daher nicht einfach in ihnen auf-oder absteigen."

We do not think that observations of a similar character can throw any additional light on this subject. The experiments which follow prove the existence and the function of these foramina between the ventricles and the subarachnoid space.

I. THE DEMONSTRATION OF FUNCTIONAL COMMUNICATION

When phenolsulphonephthalein is introduced into the ventricles, it appears in the spinal fluid in from one to seven minutes. In these cases there was no increased tension of the ventricular fluid and no pressure was used. The results can therefore be attributed only to the normal means of regulating the distribution of fluids. The time of appearance of the dye in the spinal fluid may occasionally be delayed in cases of hydrocephalus even when there is free communication (Case 3).

TABLE 4.—TIME OF APPEARANCE OF PHENOLSULPHONEPHTHALEIN IN THE SUBARACHNOID SPACE FOLLOWING ITS INTRODUCTION INTO THE VENTRICLES

Case 1.....	2 minutes
Case 2.....	7 minutes
Case 3.....	{ 13 minutes 20 minutes
.....	
Case 4.....	1 minute

When phenolsulphonephthalein is substituted for an equal amount of *spinal fluid* and introduced into the spinal subarachnoid space, the dye is soon found *in the ventricles*. These observations demonstrate that an open communication exists between the ventricles and the subarachnoid space in both directions. They also demonstrate that fluid readily passes upward into the ventricles even against the stream of cerebrospinal fluid from the ventricles. Such results render untenable the theory, usually credited to Key and Retzius and recently advocated by Propping, that valves, though not demonstrable, exist at these openings. The passage of fluids from the subarachnoid space into the ventricles is of the greatest importance in its bearing on intraspinal anesthesia and the treatment of diseases of the central nervous system by intraspinal injections.

II. THE LOCATION OF THE COMMUNICATION

If an obstruction exists either at the aqueduct of Sylvius or at the basal foramina of Magendie and Luschka, phenolsulphonephthalein, after introduction into the ventricles, does not appear in the spinal fluid. This was the case in seven patients, and the obstruction was found in four on whom post-mortem examination was held.

This proves that there are no openings between the third and lateral ventricles and the subarachnoid space, or in other words, that the foramina of Bichat and Mierzejewsky (or the lateral foramina of Bichat) do not exist. The aqueduct of Sylvius is the only channel for the escape of fluid from the third and lateral ventricles. The openings between the ventricles and the subarachnoid space must therefore be posterior to the aqueduct of Sylvius and must lead from the fourth ventricle. These openings are the foramina of Magendie and Luschka.

7. *THE DISTRIBUTION OF GRANULES IN THE SUBARACHNOID SPACE*

Those who favor the theory of absorption of cerebrospinal fluid by means of stomata or by specialized structures along the longitudinal or other sinuses have assumed the presence of an intra-arachnoidal current to carry the cerebrospinal fluid to these structures. This is very similar to the assumption that an intraperitoneal current carries the fluids to the central tendon of the diaphragm. We have been unable to find any evidence to support such an assertion either in the peritoneal cavity (Dandy and Rowntree) or in the subarachnoid space.

To determine the presence or absence of a current in the subarachnoid space, we substituted for the cerebrospinal fluid (withdrawn through the occipito-atlantal membrane) an equal amount of a suspension of lampblack granules. The animal was kept under anesthesia from one to two hours, and at the end of this time was killed and frozen to avoid distribution of the granules after death. Subsequent examination showed a most uniform distribution of granules throughout both the cerebral and spinal subarachnoid space. In so far as could be determined there was absolutely no evidence of any accumulation along the sinuses or in any other locality. With the exception of four parts of cranial nerves, there were no granules along the nerve sheaths. Granules were present in the olfactory nerves to their termination, the optic nerves to the fundus, the trigeminus over the gasserian ganglion and the auditory nerve to the internal auditory meatus. This distribution represents the normal limits of the distribution of the cerebrospinal fluid. If pressure is used, and only then, the other cranial and spinal nerves may be injected for varying distances.

The even and quite rapid distribution of granules throughout the cerebrospinal fluid is more readily explained by the pulsation in the central nervous system.

Part 2.—Clinical and Pathological Studies

In the following observations we determined the amount of absorption from the ventricles, the amount of absorption from the subarachnoid space and whether or not there was free communication between the ventricles and the subarachnoid space. Phenolsulphonephthalein⁵ was used in these studies. After the introduction of a phenolsulphonephthalein solution into the ventricles and, at a subsequent test, into the subarachnoid space, the time of its first appearance in the urine was determined and the amount which was excreted in the urine for a two-hour period was estimated. The patency or occlu-

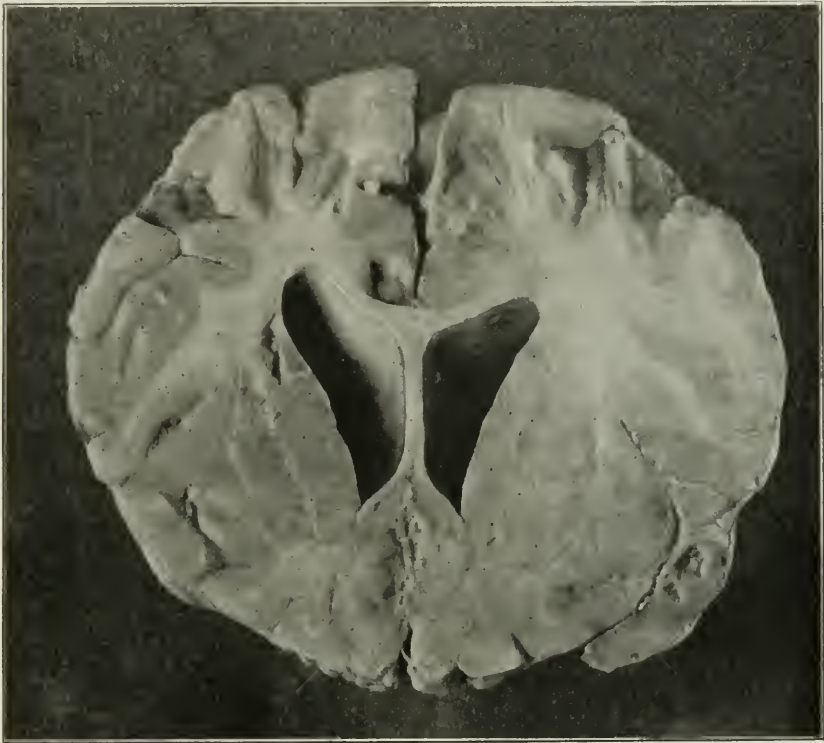


Fig. 8.—Brain, cross-section of a normal child of 1 year; included as a standard for comparison with specimens of internal hydrocephalus which follow.

5. It should be emphasized that the ordinary solution of phenolsulphonephthalein is made up with alkali; this is sufficient to prevent its use in the central nervous system. We used a neutral solution which, when diluted with cerebrospinal fluid, caused no symptoms whatever referable to the central nervous system. For ventricular use, 1 c.c. (6 mg.) of phenolsulphonephthalein was diluted with 3 c.c. of cerebrospinal fluid and for spinal subarachnoid use 1 c.c. (6 mg.) of phenolsulphonephthalein was diluted with 2 c.c. of cerebrospinal fluid.

sion of the communication was determined by the presence or absence in the spinal fluid of the phenolsulphonephthalein after its introduction into the ventricles.

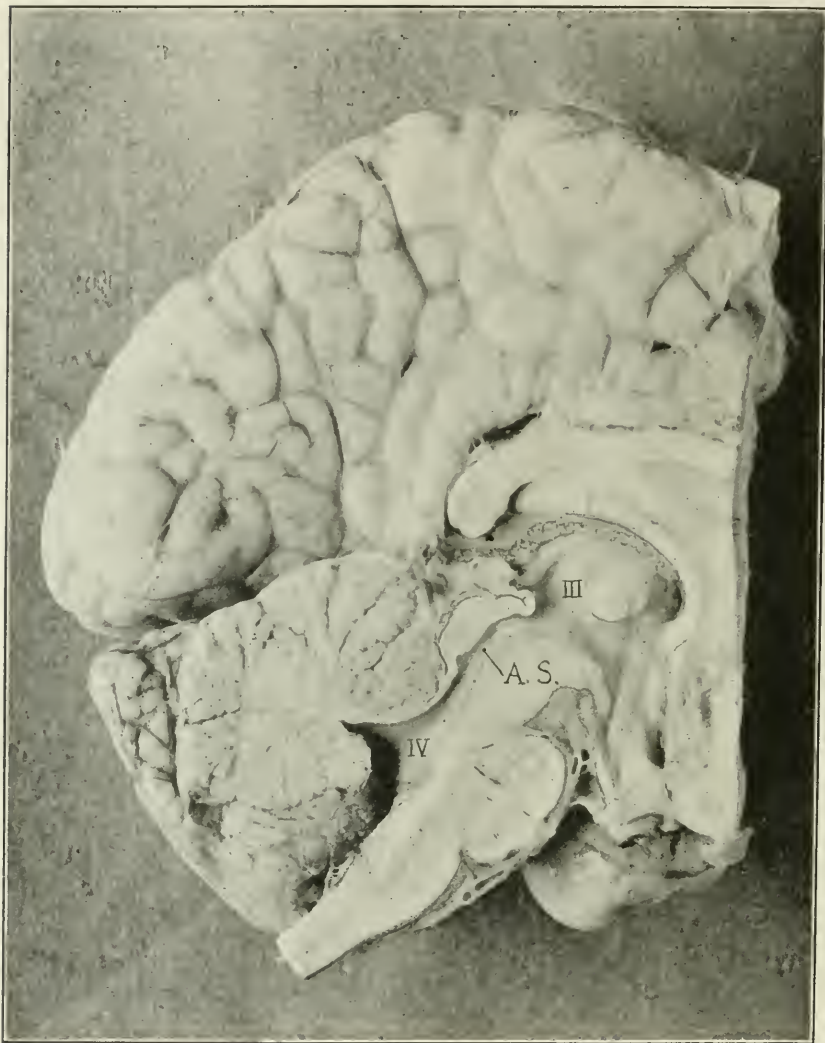


Fig. 9.—Midsagittal section of brain shown in Figure 8. Note the patent foramen of Magendie and the aqueduct of Sylvius.

8. *ABSORPTION FROM THE VENTRICLES AND THE SUBARACHNOID SPACE WHEN HYDROCEPHALUS DOES NOT EXIST*

In a number of patients in whom a ventricular or lumbar puncture was indicated for diagnosis, phenolsulphonephthalein was substituted

for the cerebrospinal fluid removed. From these results a normal standard of absorption from the ventricles and the subarachnoid space and the average time of normal communication between them were obtained.

It was found that after introduction into the ventricles, phenolsulphonephthalein appeared in the urine *in from ten to twelve minutes, and that during two hours from 12 to 20 per cent. was excreted.* When introduced into the subarachnoid space it appeared in the urine *in from six to eight minutes, and from 35 to 60 per cent. was excreted in two hours.* Phenolsulphonephthalein passed rapidly from the ventricles to the subarachnoid space, and appeared in the spinal fluid *in from one to three minutes.*

Pathological studies have shown that in some cases of hydrocephalus the communication between the ventricles and the subarachnoid space is open and that in others it is closed. It is obvious that a different operative procedure is indicated in these different types of cases. The inability to decide which type is present is undoubtedly one reason why the results of operation have been so unsatisfactory. We have endeavored to determine the presence or absence of the communication in hydrocephalus by the use of phenolsulphonephthalein after having demonstrated on animals that the method was harmless. In all cases permission for applying the tests was obtained from the parents.

9. STUDIES OF THE ABSORPTION FROM THE VENTRICLES AND THE SUBARACHNOID SPACE IN PATIENTS WITH INTERNAL HYDROCEPHALUS

It was possible to divide the cases which we studied into two groups. The introduction of phenolsulphonephthalein into the ventricles and a later examination for this substance in the spinal fluid will determine either by its absence that the communicating foramina are occluded (Group 1) or by its presence that they are patent (Group 2).

GROUP 1.—INTERNAL HYDROCEPHALUS WITH OBSTRUCTION TO THE CHANNELS OF EXIT FROM THE VENTRICLES

CASE 1.—P. G., aged 7 months. Diagnosis: General miliary tuberculosis, tuberculous meningitis; internal hydrocephalus secondary to meningitis; meningocele.

Clinical Note.—Family History: Two other children living and well. No family history of hydrocephalus.

Past History: Full term, normal delivery. The patient was born with a meningocele. Dentition began at 3 months. Sat up at fourth month. No acute illness. No apparent disturbance from meningocele.

Present Illness: The patient had a severe cough and fever and had been very drowsy for a week.

Physical Examination: The patient was a well-nourished infant lying in a state of coma. In the sacral region was a large meningocele. Compression of the tumor caused bulging of the anterior fontanel. Von Pirquet test, positive.

Spinal Fluid from Meningocele: Clear fluid, 112 cells per cubic millimeter; tubercle bacilli present.

Tests.—1. There was no evidence of communication between the ventricles and the spinal subarachnoid space in forty-five minutes. 2. After ventricular introduction phenolsulphonephthalein did not appear in the urine for forty-five minutes. *In two hours only 0.75 per cent. was excreted.* It was being excreted seventy hours later. 3. The absorption from the spinal subarachnoid space was

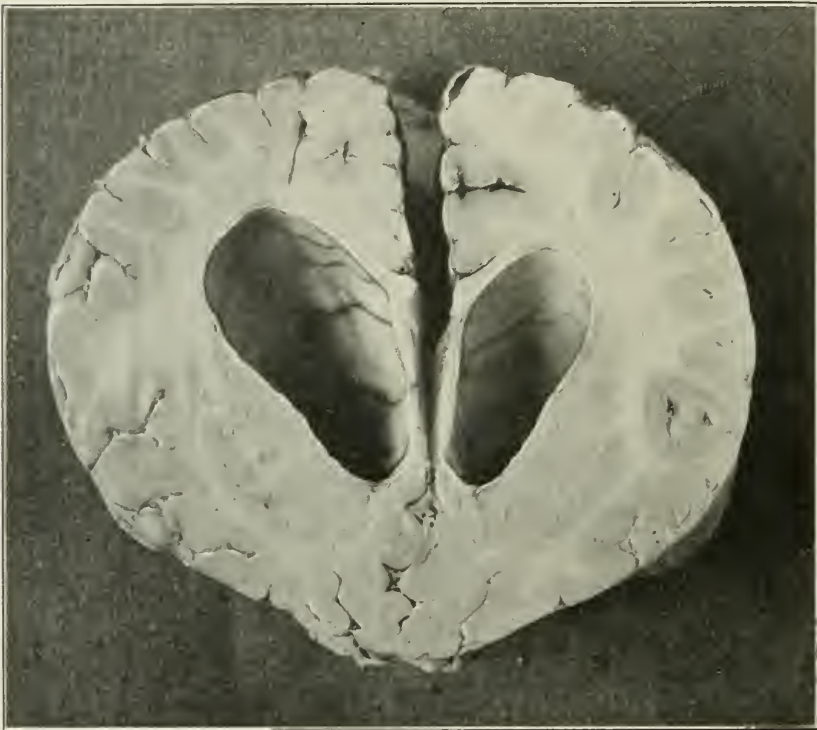


Fig. 10.—Cross-section of brain, showing moderately dilated lateral ventricles, in acute internal hydrocephalus (Case 1, Group 1, P. G.) due to occlusion of the foramina of Magendie and Luschka by a tuberculous exudate. There was no absorption from the ventricles.

rapid. Phenolsulphonephthalein first appeared in the urine six minutes after its introduction into the ventricles, and *62 per cent. was excreted in the first two hours.*

Death from tuberculous meningitis.

Pathological Findings.—General miliary tuberculosis; tuberculous meningitis; myelomeningocele; internal hydrocephalus. The brain was normal in size. There was a plastic exudate over both parietal lobes, along the falx cerebri and the sylvian arteries, and scattered over the cerebral cortex were numerous tubercles. The base of the brain was covered with a thick exudate which extended from the optic chiasm posteriorly over the inferior surface of the

pons and medulla, and the lower surface of both cerebellar hemispheres. The cisterna magna was filled with exudate. *The foramina of Magendie and foramina of Luschka were completely occluded by this exudate* (Figs. 10 and 11). On section, the ventricles were moderately dilated. A sagittal section continued through the midline showed the foramen of Monro to be moderately dilated, and the aqueduct of Sylvius patent. The fourth ventricle was about normal in size, and was partly filled with tuberculous exudate. This exudate, in addition

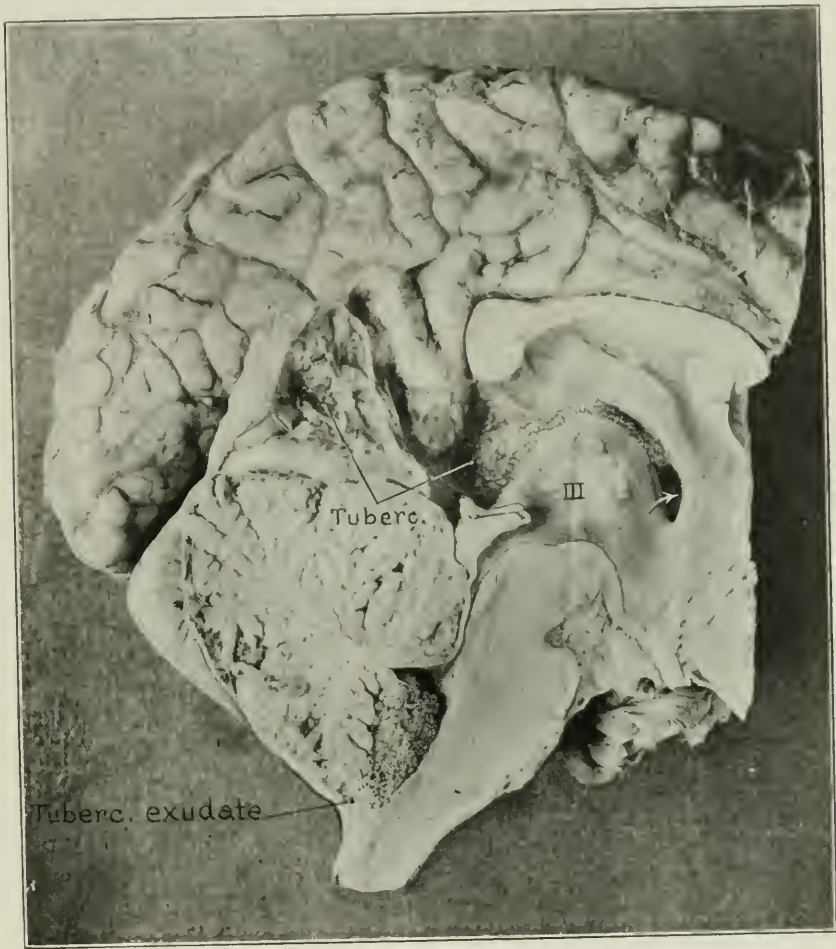


Fig. 11.—Midsagittal section of brain in Case 1. Observe the exudate which completely fills the space between the medulla and cerebellum and binds them together. This completely blocked the foramina of Magendie and Luschka. The aqueduct of Sylvius is patent.

to forming an external covering, firmly bound the medulla and the cerebellum together, thus doubly sealing the foramina of exit. It was also continuous with that which extended over the surface of the cerebellum and the base of the brain. Many tubercles were scattered over the ependyma of the third and of the lateral ventricles. The choroid plexus appeared normal except for tubercles

demonstrated histologically. The pineal gland was very small, measuring about 2 mm. in diameter. The vein of Galen was patent.

The spinal cord and its meninges did not appear abnormal, except for a few miliary tubercles; no exudate was present. *Meningocele*: The sac measured 8 by 7 cm. It projected through a median defect in the first and second sacral vertebrae and was firmly attached to the bodies of these vertebrae by a small pedicle 1.5 cm. in length. The cord ended at the upper part of the meningocele; the filum terminale and a few branches of the cauda crossed the cavity of the meningocele and became embedded in a cicatrix on the dorsal wall. The sac of the meningocele was directly continuous with the subarachnoid space.

CASE 2.—A. H., aged 6 months. Diagnosis: Internal hydrocephalus, myelomeningocele (ruptured).

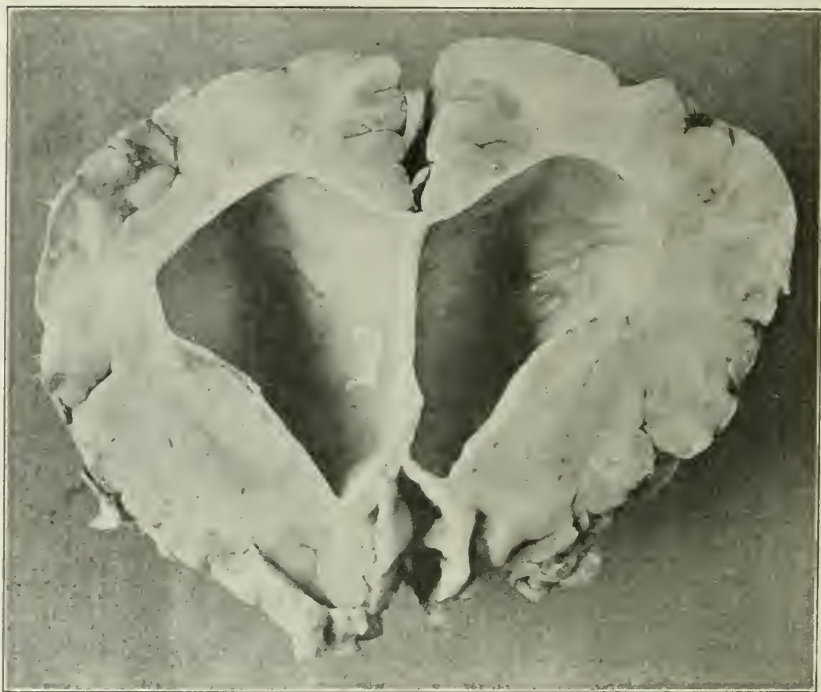


Fig. 12.—Cross-section of brain to show greatly distended lateral ventricles in case of internal hydrocephalus (Case 2, Group 1, A. H.) due to complete occlusion of the aqueduct of Sylvius.

Clinical Note.—Past History and Present Illness: Only child, full term, normal delivery. At birth the mother noticed a "swelling" the size of an apple over the lower part of the spine (meningocele), and the head appeared to be larger than normal. The baby had never moved her legs. The head and the swelling on the back had steadily increased in size. Three days before admission the meningocele ruptured, after which there was a discharge of slightly blood-tinged fluid with consequent diminution in the size and in the tension of the sac.

Physical Examination: The patient was a fairly well-nourished infant with a moderate degree of hydrocephalus. The head measured 40 cm. in circumference. The anterior and posterior fontanels and the sutures were widely open.

There was a downward dislocation of the eyes and a nystagmus in all directions. The neck was rigid and the arms slightly spastic. The lower extremities were flaccid and atrophied; the reflexes were absent. A collapsed meningocele sac was present in the lower lumbar and sacral region. From the ruptured medullovascular area a turbid, slightly blood-tinged fluid exuded.

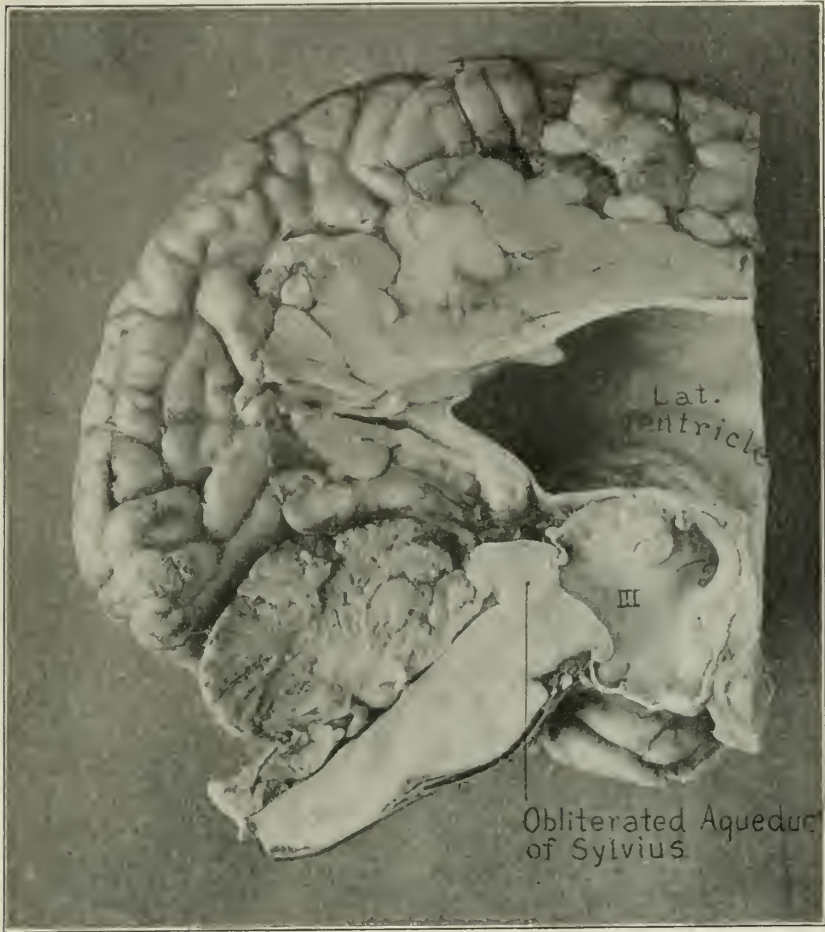


Fig. 13.—Midsagittal section of brain in Case 2 to show complete absence of the aqueduct of Sylvius and its replacement by neuroglia. Note the greatly dilated third and lateral ventricles anterior to the obstruction and the flattened slit-like fourth ventricle posterior to the obstruction. The septum lucidum is almost completely atrophied.

Tests.—1. There was no evidence of communication between the ventricles and the spinal subarachnoid space in two hours. 2. Forty minutes after ventricular introduction of phenolsulphonephthalein it had not appeared in the urine. In two hours only 1 per cent. was excreted in the urine.

Death occurred as a result of the rupture of the meningocele sac.

Pathological Findings.—The brain was enlarged. The sulci were shallow and the convolutions flattened. The meninges appeared normal, the foramina of Luschka and Magendie were patent. The lateral and third ventricles were greatly and uniformly dilated, the relative and absolute size of which are shown in the photographs (Figs. 12 and 13). The fourth ventricle was flattened to a mere slit.

The aqueduct of Sylvius was completely obliterated. There was a small blind pouch at the position where the aqueduct should begin from the third ventricle, but beyond this there was no gross evidence of its presence. Cross

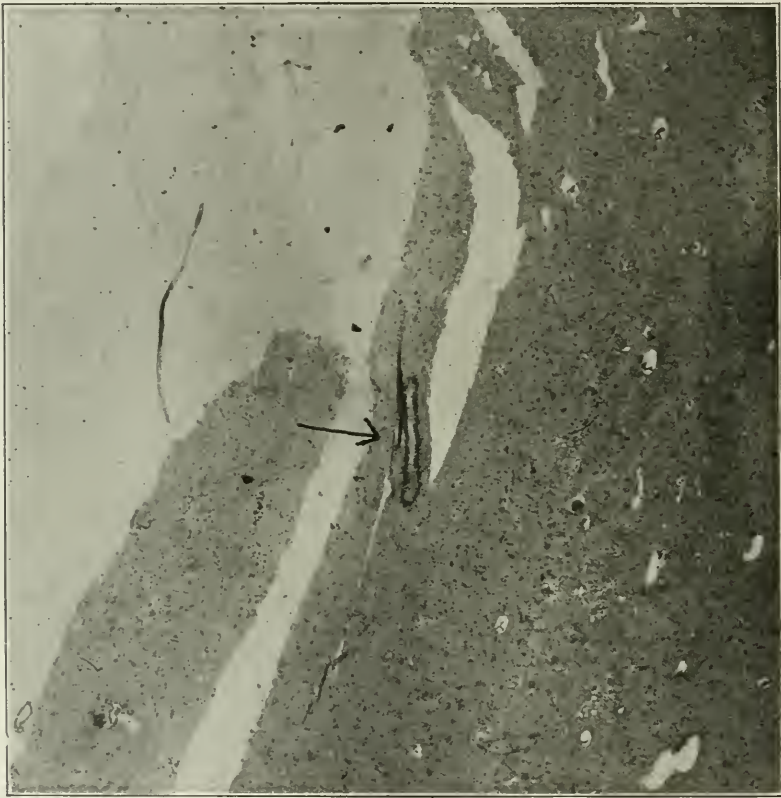


Fig. 14.—Photomicrograph to show a microscopic remnant of the aqueduct of Sylvius in Case 2.

sections of the midbrain examined microscopically showed two independent, small spaces with a lining of ependymal cells. In one there was a small lumen and in the other the walls were in apposition. They undoubtedly represented remains of the aqueduct of Sylvius (Fig. 14). Microscopically there was a gliosis which had replaced the aqueduct of Sylvius. The corpora quadrigemina were very large but symmetrical.

The vena Galena magna was normal in size and the lumen was patent. The pineal gland was small. The choroid plexuses of the lateral ventricles were normal.

The meningocele sac measured 10 by 7 by 6 cm. It protruded through a defect in all the lumbar and the first sacral vertebrae and was attached by a broad base to these vertebrae. Its cavity was directly continuous with the subarachnoid space of the spinal cord. A series of from six to seven nerve roots rising from the cord at the line of attachment to the vertebrae ran transversely, on each side, through the cavity to the walls of the sac.

The spinal canal and subarachnoid space were otherwise normal.

Remarks.—The absence of communication was shown by the tests. This was substantiated by finding only microscopic remnants of the aqueduct of Sylvius. The dilatation of the third and lateral ventricles ahead of the obstruction and the collapsed fourth ventricle behind the obstruction were evidences of the influence of an obstruction in the aqueduct.

CASE 3.—N. P., aged 6 weeks. Diagnosis: Internal hydrocephalus.

Clinical Note.—Family History: Two other children aged 2 years and 4 years living and well. No history of syphilis or hydrocephalus.

Past History and Present Illness: Full term, normal delivery. At birth it was noticed that the child's head was large. When 2 weeks old she had general convulsions which lasted two or three days. Three weeks before death she had convulsions lasting over a period of three or four days. The head had grown progressively larger.

Physical Examination: The patient was an emaciated infant with hydrocephalus. The head measured 50.5 cm. in circumference. There was separation of nearly all of the cranial bones. There was displacement of the eyes downward and a nystagmus in all directions.

Tests.—1. There was no evidence of communication between the ventricles and the subarachnoid space in twenty minutes. 2. After ventricular introduction phenolsulphonephthalein did not appear in the urine in forty-five minutes. During two hours only 1 per cent. was excreted.

Death from internal hydrocephalus.

Pathological Findings.—The cortex in places was only a millimeter in thickness and the brain collapsed into a shapeless mass when it ruptured. Sulci were present only over the temporal lobes; the remaining cortex was smooth. The size of the ventricles was almost equal to that of the calvarium. The foramina of Monro were from five to six times the normal size. There was complete atrophy of the septum lucidum. The fourth ventricle and the basal foramina of Luschka and Magendie were normal; the meninges were normal; the cerebellum was greatly flattened anteroposteriorly, as the result of the pressure of fluid in the lateral ventricles.

There was no aqueduct of Sylvius (Fig. 15). No trace of the aqueduct of Sylvius could be found in the gross or in sections when examined under the microscope, nor was there any evidence of epithelial remains as in the previous specimen. The choroid plexus was small but otherwise appeared normal. The vein of Galen was unobstructed. The pineal body was small. The spinal cord and the meninges, cerebral and spinal, were normal.

CASE 4.—N. M., aged 24 months. Diagnosis: Internal hydrocephalus.

Clinical Note.—Family History: Three other children living and well. No history of hydrocephalus or syphilis.

Past History and Present Illness: Full term, normal delivery. The patient's head was "large and round" at birth, but until he was 4½ months old it was not considered abnormal in size. He never held up his head, sat up or walked. Dentition began at the twelfth month. The patient had had no illness suggestive of meningitis. A puncture of the corpus callosum was performed when the patient was 1 year old. The head continued to increase in size.

Physical Examination: The patient was a well-nourished child, with a very large head, which measured 54 cm. in circumference. The anterior fontanel was 10 by 9 cm. in diameter; it was tense and bulging. The sutures were widely

separated. There was ocular displacement downward, an internal strabismus of the left eye and a nystagmus in all directions. The eye-grounds showed optic atrophy. There was a slight spasticity of the arms and legs. The reflexes were exaggerated and there was an ankle clonus. The head increased 11 cm. in seven months. The child's condition otherwise remained the same except for a partial weakness of both arms and legs.

Blood: Wassermann reaction, negative.

Ventricular Fluid: Clear. Noguchi globulin reaction negative, 6 cells per cubic centimeter.

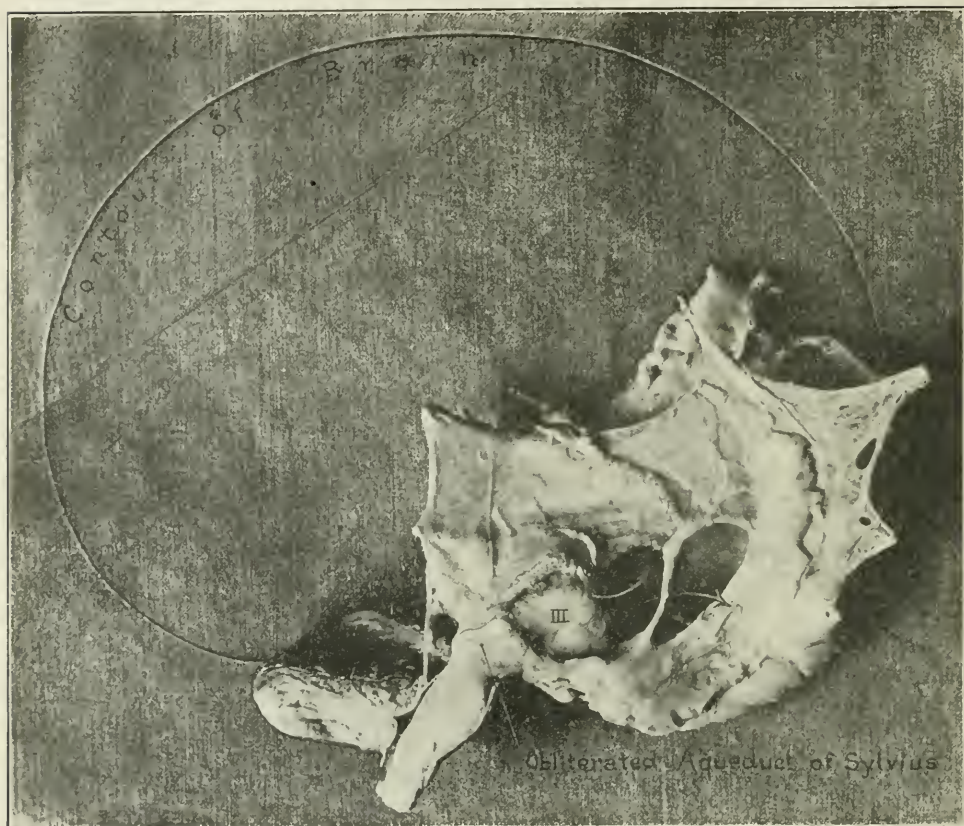


Fig. 15.—Advanced internal hydrocephalus (Case 3, Group 1, N. P.) caused by a completely occluded aqueduct of Sylvius. The cortex is a mere shell and could not be retained in its proper form. Note the exceedingly large foramen of Monro and the fringes of choroid plexus. Note the small fourth ventricle behind the occluded aqueduct of Sylvius, in marked contrast to the huge ventricles in front of this obstruction. The cerebellum is greatly flattened from the pressure of the distended lateral ventricles.

Tests.—1. There was no evidence of communication between the ventricles and the subarachnoid space in two days. 2. After ventricular introduction phenolsulphonephthalein did not appear in the urine for forty minutes. In two hours only 0.6 per cent. was excreted. Phenolsulphonephthalein was being excreted after eleven days. One month later, similar results were obtained.

Phenolsulphonephthalein appeared in the urine in thirty-five minutes and 0.5 per cent. was excreted in two hours. It was being excreted after eleven days. 3. After subarachnoid introduction, phenolsulphonephthalein appeared in the urine in six minutes, and 35 per cent. was excreted in two hours. After twenty hours there was no trace of phenolsulphonephthalein in the urine. 4. The kidney function was normal; 45 per cent. was excreted in two hours.

Remarks.—The results in this case were very similar to the one preceding: there was practically no absorption from the ventricle, and the appearance time of phenolsulphonephthalein in the urine was greatly delayed. In marked contrast were the results obtained from the subarachnoid space. It was evident that there was no communication between the ventricles and the subarachnoid space. The duration of excretion over eleven days in two separate experiments demonstrated the slow rate of absorption from the ventricles.

There could be no doubt that an obstruction existed either at the aqueduct of Sylvius or the basal foramina of Luschka and Magendie. We were never able to obtain more than 3 c.c. of cerebrospinal fluid by lumbar puncture. From the fact that so little spinal fluid could be obtained, we were inclined to infer that the obstruction was located at the basal foramina.

The patient is living.

CASE 5.—M. R., aged 13 months. Diagnosis: Internal hydrocephalus.

Clinical Note.—Family History: Mother and father living and well. The patient was a third child; a brother aged 5 years and a sister aged 3 living and well. No history of syphilis; no history of hydrocephalus.

Past History and Present Illness: The child was born at full term; instrumental delivery. The patient was well until 4 months old. Then she had a severe illness, which lasted one month. The body was rigid; there was marked opisthotonus and many convulsions of a general character; during this time the patient had a high fever. The mother noticed an enlargement of the head three weeks after the onset of this illness. The following four months, the increase in the size of the head was rapid. After that it grew larger but not so rapidly.

Examination: The patient was a well-nourished child. The head measured 55.5 cm. in circumference. The fontanelles were open. The sutures were widely separated. There was marked downward displacement of the eyes, so that the pupils were almost entirely hidden behind the lower lids. A lateral and vertical nystagmus was present. There was a low grade (1 to 2 diopters) bilateral choked disk. Von Pirquet test, negative.

Spinal Fluid: Clear, six cells per cubic centimeter; Wassermann, negative. Reducing substance (Fehling's), present.

Ventricular Fluid: Five c.c. clear fluid, two cells per cubic millimeter; Wassermann, negative; reducing substance (Fehling's), present.

Tests.—1. There was no evidence of communication between the ventricles and the subarachnoid space in one and one-half hours. 2. After ventricular introduction, phenolsulphonephthalein did not appear in the urine for twenty minutes. Only 0.9 per cent. was excreted in two hours. 3. After subarachnoid introduction, phenolsulphonephthalein appeared in the urine in eight minutes; 25 per cent. was excreted in two hours.

Patient died two months later of hydrocephalus.

Pathological Findings.—The brain was hardened *in situ* with formaldehyde solution. When removing the brain, an unusual accumulation of fluid filling the entire posterior cranial fossa was encountered. This could be likened to an encapsulated cyst. The walls were thin, transparent and in many places adherent to the dura. While freeing the lateral portions of the cyst, it was punctured and the brain collapsed. The cyst was a greatly dilated fourth ventricle, and the roof of the ventricle formed its walls (Fig. 16). Its size was limited only by the limitations of the posterior fossa. The cyst wall was adherent to the spinal cord and the lateral lobes of the cerebellum, making an impermeable membrane and preventing communication between the ventricles and the suba-

rachnoid space. The lateral lobes of the cerebellum were separated 4 cm. and between them stretched this impermeable membrane. The aqueduct of Sylvius was considerably dilated. The septum lucidum was atrophied; the third and lateral ventricles and the foramina of Monro were greatly dilated. Their relative size is best shown in the accompanying drawings⁶ (Figs. 17 and 18).

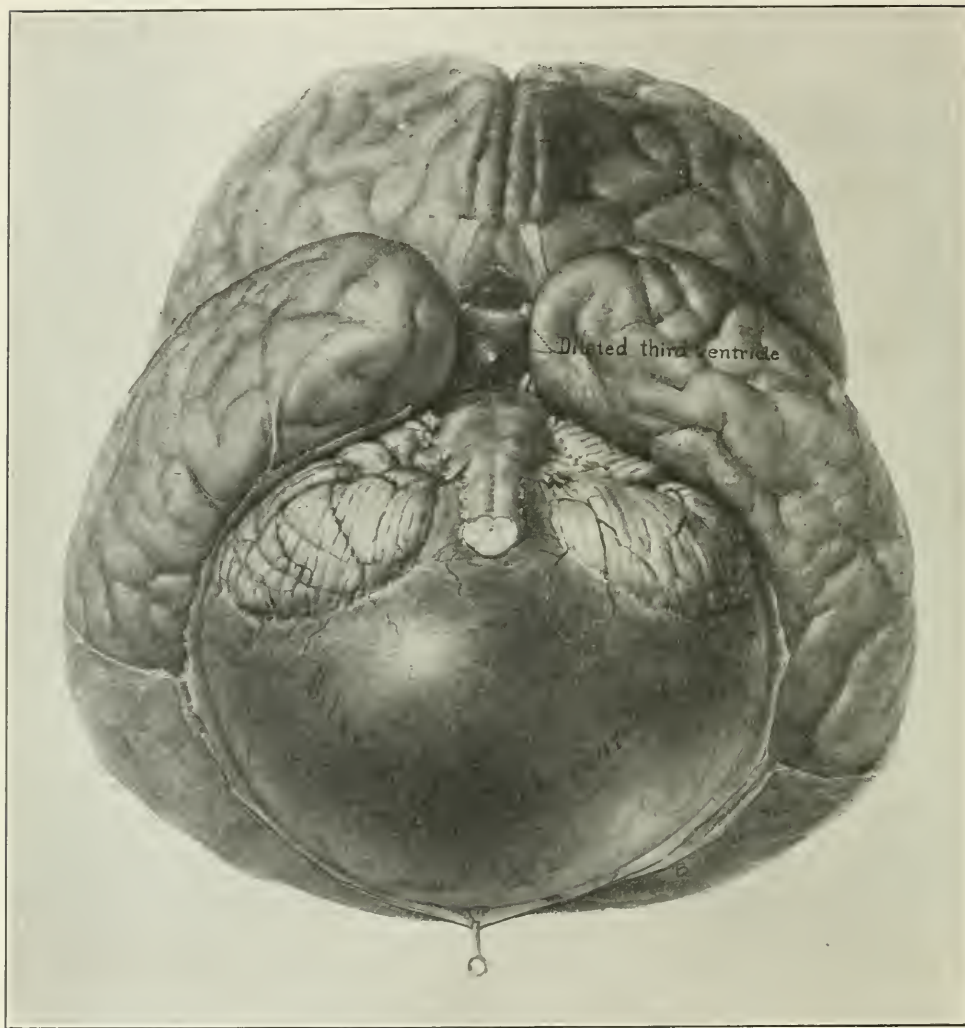


Fig. 16.—Ventral view of the brain in Case 5, Group 1, M. R. The foramina of Magendie and Luschka are absent and the fourth ventricle is distended into a huge cyst completely filling the posterior cranial fossa. The lateral lobes of the cerebellum are separated and crowded to either side. Note also the distended third ventricle.

6. We wish to express our thanks to Mr. Max Brödel for the accompanying drawings and for his assistance in the preparation of many of the figures.

The pia arachnoid was everywhere fused with the "cyst wall" of the fourth ventricle; this membrane was greatly thickened over the base of the brain. The usual transparent bridge of the pia arachnoid between the inferior surface of the pons and the optic chiasm was so opaque that the underlying brain was invisible; this opaque thickened membrane was also continuous over and adherent to the floor of the third ventricle. It also completely covered and was

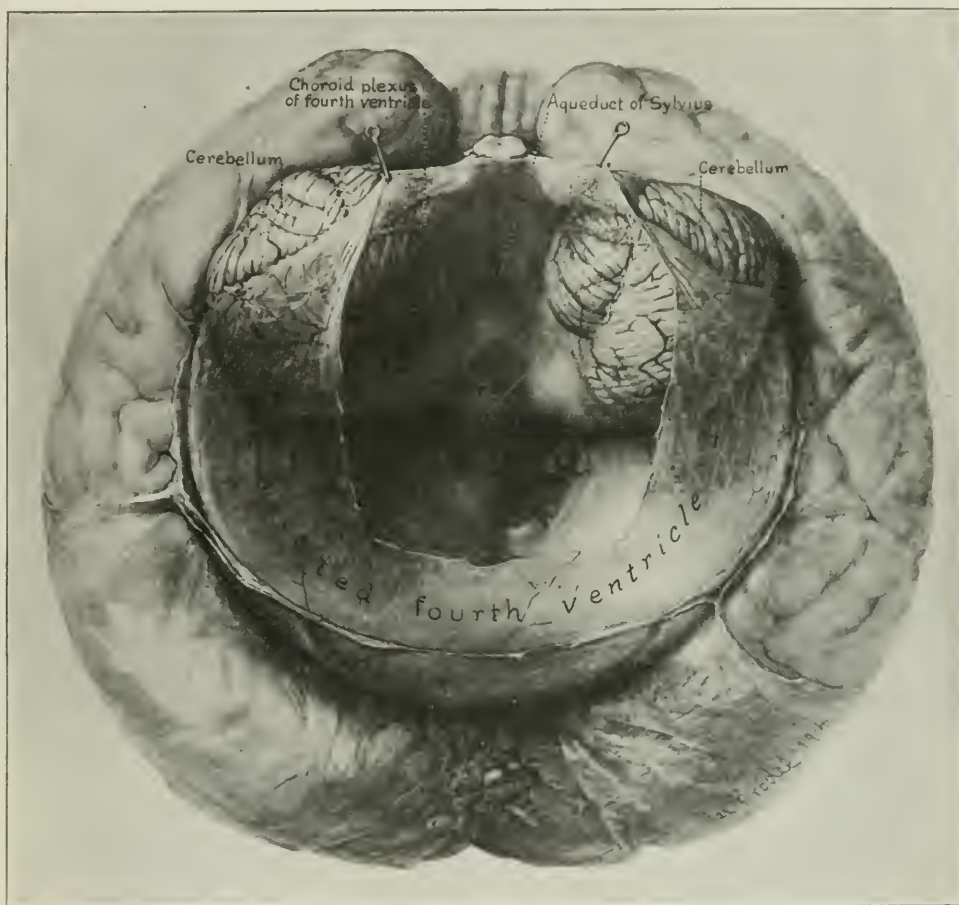


Fig. 17.—View of dilated fourth ventricle in Case 5 with window removed. Note the extent of the "cyst," the separation of the cerebellar hemispheres and the patent aqueduct of Sylvius.

adherent to the optic chiasm. Over the entire base of the brain this thickening of the meninges was very apparent; over the surface of the cerebral lobes it was less apparent.

The vein of Galen and the straight sinus were normal; the choroid plexuses appeared to be normal. The choroid plexus of the fourth ventricle was entirely within the cyst. The pineal gland was small. The spinal cord was not obtained for examination.

Remarks.—In this case also an absence of communication was demonstrated by the phenolsulphonephthalein test. This was confirmed by the post-mortem findings. There was practically no absorption from the ventricles and a rather high though subnormal absorption from the subarachnoid space. The partial obliteration by adhesions of the subarachnoid space over these areas mentioned no doubt explains the diminished absorption from this space.

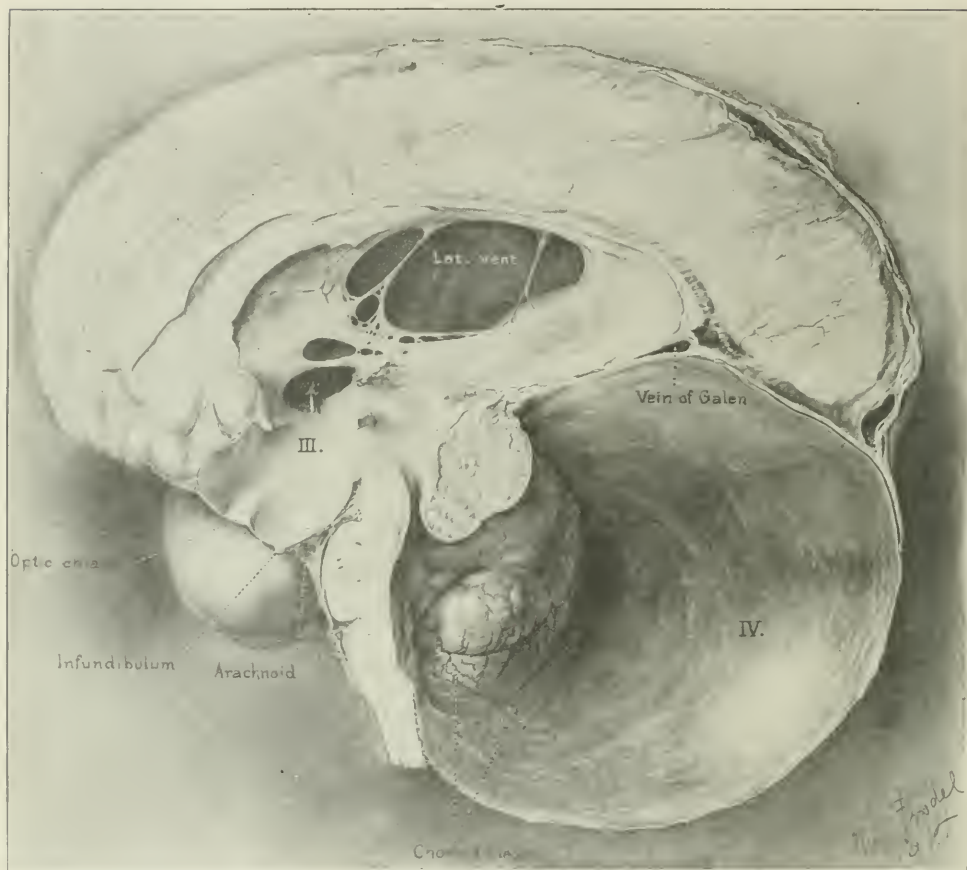


Fig. 18.—Midsagittal view of brain in Case 5. All the ventricles communicate freely with each other. There are no foramina of Magendie and Luschka. The choroid plexus is included in the "cyst." Note the patent and enlarged foramen of Monro (arrow) and aqueduct of Sylvius. The large openings in the septum lucidum show the effects of the intraventricular pressure.

CASE 6.—F. W., aged 6 months. Diagnosis: Internal hydrocephalus. Meningocele and syringomyelocele.

Clinical Note.—Family History: The patient was the youngest of four children. The other three were well. There was no evidence of syphilis. No history of hydrocephalus.

Past History: Full term, difficult delivery, owing to large head, without instruments. Weight at birth, 10 pounds.

Present Illness: The mother noticed that the head was abnormally large at birth. There was also present a large "swelling" over the middle of the lower back. The circumference of the head and the swelling over the back gradually increased in size.

Examination: The patient was a well-nourished infant whose head measured 51 cm. in circumference. There was diastasis of the cranial bones. The anterior and posterior fontanelles were widely open and tense. A large meningocele protruded from a spina bifida of the lower lumbar and all the sacral vertebrae. There was complete paralysis of the lower extremities. The head grew 5 cm. in one month.

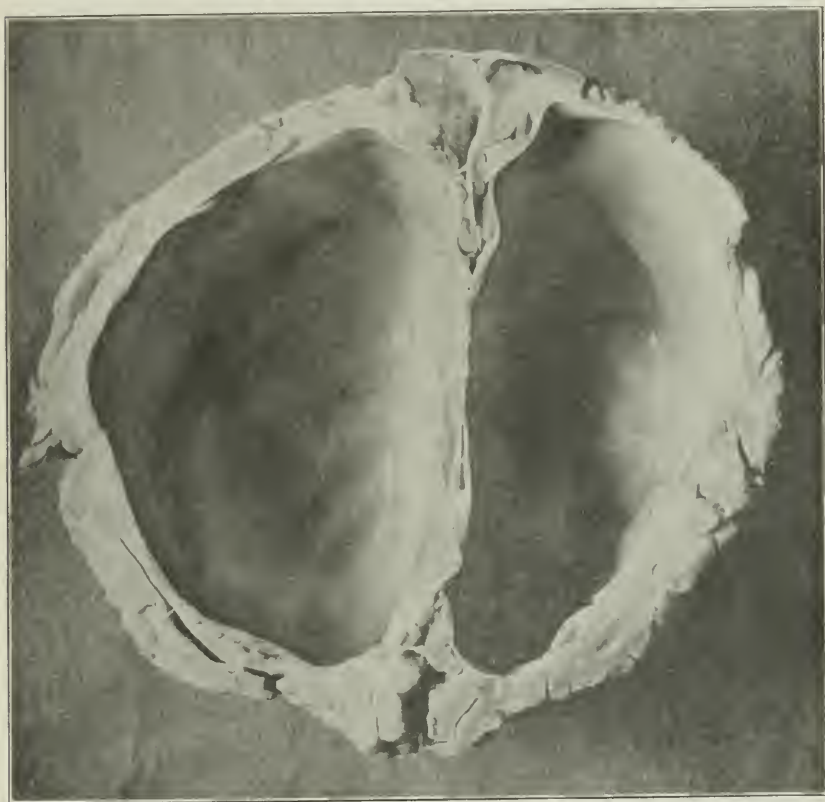


Fig. 19.—A very advanced internal hydrocephalus (Case 6, Group 1, F. W.) due to inflammatory adhesions at the base, which occluded the foramina of Magendie and Luschka.

Spinal Fluid: Clear, 3 cells per cubic millimeter. Noguchi globulin reaction negative. Reducing substance present (Fehling's).

Ventricular Fluid: Clear, 2 cells per cubic millimeter. Noguchi globulin reaction negative. Reducing substance present (Fehling's).

Tests.—1. There was very slight evidence of communication between the ventricles and the subarachnoid space in four and one-half hours. A faint trace of phenolsulphonephthalein was then present. 2. After ventricular introduction, phenolsulphonephthalein did not appear in the urine for sixteen minutes. Two per cent. was excreted in two hours. The head increased in size and at a test

after two months there was only 1 per cent. excreted in two hours. Phenolsulphonephthalein appeared in the urine in twenty-five minutes. At this time there was no evidence of communication between the ventricles and the subarachnoid space after three hours. 3. After subarachnoid introduction, phenolsulphonephthalein appeared in the urine in twelve minutes, and 10 per cent. was excreted in two hours. 4. The kidney function was normal.

The patient died of hydrocephalus.



Fig. 20.—Cross-section of brain in Case 6, to show extreme ventricular enlargement, aqueduct of Sylvius patent. Dilatation of the fourth ventricle was prevented by adhesions between the dura and the cerebellum.

Pathological Findings.—The dura was firmly adherent to the cerebellum by fibrous bands, which had to be torn before the brain could be removed. These adhesions were present throughout the posterior fossa and extended almost the entire distance of the spinal canal, binding the spinal cord to the dura. The cerebellum was also firmly bound to the medulla by adhesions which occluded the foramina of exit from the fourth ventricle (Figs. 19 and 20).

The cerebral cortex was so thin that in places it was translucent. This was especially true over the temporal lobes. Here no convolutions were evident, the surface being entirely smooth. The convolutions were elsewhere flattened and the sulci shallow. Viewed from below the floor of the third ventricle appeared as a film. The third and lateral ventricles and the foramina of Monro were greatly dilated; only shreds of the septum lucidum remained. The aqueduct of Sylvius was about normal in size and everywhere patent. The fourth ventricle was compressed. The first portion of the central canal of the cord was dilated, but this soon became obliterated so that throughout its entire length there was no connection with the syringomyelocoele. When the ventricles were filled, the fluid readily passed out of the central canal but not through the foramina of Luschka and Magendie. These were entirely occluded.

The corpora quadrigemina were very large. The pineal gland was small. The choroid plexus appeared normal in the gross. Microscopically the choroidal epithelium was flattened and the vascular spaces somewhat dilated.

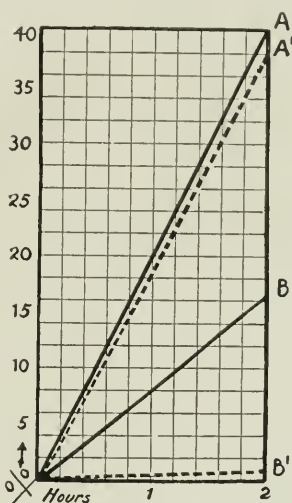


Fig. 21.—Curves comparing the normal absorption from the ventricles and the subarachnoid space with the absorption in internal hydrocephalus of the obstructive type. The base line represents a two-hour interval and the vertical line the percentage of absorption (excretion of phenolsulphonephthalein) during that time. The heavy lines represent the normal absorption and the dotted lines the absorption in hydrocephalus. *A*, normal subarachnoid absorption; *A'*, absorption from subarachnoid space of case of obstructive hydrocephalus; *B*, normal absorption of fluid placed in the ventricles; *B'*, absorption from ventricles in obstructive hydrocephalus.

Syringomyelocoele and Meningocoele: Two separate, non-communicating cavities were contained within the cutaneous covering. The sac protruded through a defect in the third, fourth and fifth lumbar and all the sacral vertebrae. The walls of the sac were fused in part. The meningocoele was in communication with the subarachnoid space and contained clear fluid. The syringomyelocoele was connected for a short distance with the central canal of the cord. This cavity contained turbid straw-colored fluid. The central canal of the cord was obliterated between the syringomyelocoele and the medulla. At those points, the canal was greatly dilated. There was no communication between the cerebral ventricles and the syringomyelocoele.

Remarks.—This case is unusual in that at first a very slight communication existed between the ventricles and the subarachnoid space. One month later and shortly before death there was no evident communication in three hours, and absorption following ventricular injection had diminished to 1 per cent. The time of appearance in the urine increased to twenty-five minutes.

The subarachnoid absorption was low (10 per cent.). An old inflammatory process was present obliterating all the basal foramina and tightly binding the

TABLE 5.—SUMMARY OF GROUP 1, INTERNAL—

Name and No.	Patient's Illness	Absorption after Ventricular Introduction		Absorption after Spinal Introduction		Communication, Ventricle and Subarachnoid space
		Time of appearance Minutes	Two-hour absorption Per cent.	Time of appearance Minutes	Two-hour absorption Per cent.	Time of appearance
1. P. G.	Tuberculous meningitis; internal hydrocephalus	45	0.75	6	62	None in 45 min.
2. A. H.	Internal hydrocephalus	40	1	None in 2 hrs.
3. N. P.	Internal hydrocephalus	45	1	0	0	None in 20 min.
4. N. M.	Internal hydrocephalus	40	0.50	6	35	None in 2 days
		35	0.50
5. M. R.	Internal hydrocephalus	40	0.50			
		20	0.9	8	25	None in 1½ hrs.
6. F. W.	Internal hydrocephalus	16	2	12	10	Trace in less than 4½ hrs.
		25	1	None in second observation 3 hours
7. M. N.	Internal hydrocephalus	30	1.5	0	35	None in 30 min. faint trace in 14 hours

cerebellum to the medulla. This accounts for the small size of the fourth ventricle, which was unusual as the aqueduct was patent and the third and lateral ventricles were greatly dilated. On account of the strong adhesions, enlargement of the fourth ventricle was prevented. The hydrocephalus resulted from adhesions blocking the foramina of exit and preventing the cerebrospinal fluid from reaching the subarachnoid space. It must have occurred during intra-uterine life as the hydrocephalus was present at birth. Whether or not the adhesions from the inflammatory process which obliterated the cisterna were responsible for the low subarachnoid absorption can only be conjectured. This case may readily be regarded as a transitional type between those with total occlusion and those with communication (Group 2).

CASE 7.—M. N., aged 5 months. Diagnosis: Internal hydrocephalus.

Clinical Note.— Past History: The patient was born at full term after a difficult instrumental delivery. The head was not noticed to be abnormally large at birth. Paralysis of the left side of the face was observed two weeks after birth. The baby had never moved his head in a normal manner, but the parents did not attribute this to any other cause than general weakness. The head had been increasing in size for about one month.

—HYDROCEPHALUS WITH OBSTRUCTION

Duration of Excretion		Etiology	Postmortem Findings
Ventricle	Spinal canal		
3% excreted in 12 hrs. Three days later the concentration of 'phthalein in the urine was undiminished	Less than 12 hrs.	Tuberculous meningitis. Meningocele present since birth	Exudate over base of brain occluding the foramina of exit.
.....	Congenital; myelomeningocele also present	Occlusion of aqueduct of Sylvius.
.....	Congenital	Total absence of aqueduct of Sylvius.
11 days	21 hrs.	Congenital	Living.
11 days			
6.1% first 24 hours.			
7.5% second 24 hours.			
5.7% third 24 hours.			
.....	Meningitis at 4 mos. Previously normal	Absence of foramina of Luschka and Magendie. Fourth ventricle a large cyst. Marked thickening of pia arachnoid.
7 days	48 hrs.	Congenital; no history of meningitis, meningocele and syringomyelocele	Chronic inflammatory process; adhesions at base occluding foramina of exit.
.....	Congenital	Living.

Physical Examination: The patient was a fairly well-nourished infant with moderate hydrocephalus. The circumference of the head was 47.5 cm. There was downward dislocation of the eyes and a nystagmus in all directions. The eye-grounds showed a marked choking of the disks, the swelling being about 3 diopters in each fundus. The left side of the face was completely paralyzed. The extremities were normal and the reflexes at the knee active. The Wassermann reaction of the blood and spinal fluid was negative.

Ventricular Fluid: Clear, 9 cells per cubic millimeter. Globulin test, negative. Fehling's test positive.

Spinal Fluid: Clear, 5 cells per cubic millimeter. Globulin test, negative. Fehling's test positive.

Tests.—1. There was no evidence of communication between the ventricles and the subarachnoid space in thirty minutes. 2. After ventricular introduction, phenolsulphonephthalein did not appear in the urine for thirty minutes. Only 1.5 per cent. was excreted in two hours. 3. After subarachnoid introduction, 35 per cent. phenolsulphonephthalein was excreted in two hours.

Remarks.—From the results of the foregoing observations we know that there was an obstruction to the outflow of cerebrospinal fluid from the ventricles into the subarachnoid space. The excretion of phenolsulphonephthalein from the subarachnoid space (35 per cent.) was normal.

SUMMARY OF GROUP 1

The essential feature of this type of internal hydrocephalus is the absence of communication between the ventricles and the subarachnoid space. This lack of communication was demonstrated clinically in seven patients. It was confirmed at necropsy in five. In one (Case 1, P. G.) a thick tuberculous exudate covered the base of the brain and tightly sealed the communicating foramina. In two (Case 5, M. R., and Case 6, F. W.) the basal foramina were occluded by adhesions resulting from an old meningitic process; in the former, the illness occurred four months after birth, and in the latter it was evidently prenatal. In two there was complete occlusion of the aqueduct of Sylvius. In one of these (Case 2, A. H.) epithelial remnants of the aqueduct were demonstrated microscopically; in the other (Case 3, N. P.) no trace of the aqueduct was present. In both the region of the aqueduct was occupied by neuroglia tissue. The sixth and seventh patients are living (Case 4, N. M., and Case 7, M. N.). In these seven patients the absorption from the ventricle was less than 1 per cent. in six. In the one in whom the absorption was as high as 2 per cent., there was probably a minute communication between the ventricles and the subarachnoid space. At a subsequent examination the absorption in this case was less (1 per cent.), and there was proof of the obliteration of the foramina. The absorption from the ventricles is independent of the size of the ventricles or the amount of the contained cerebrospinal fluid. In Case 1 (P. G.) the ventricles were only moderately dilated and the absorption was not greater than in the most distended ventricles. The excretion of phenolsulphonephthalein in the urine is prolonged in this group (from the normal period of several hours, to ten days). The time of appearance of the dye in the urine is greatly delayed also (from thirty to fifty minutes).

In marked contrast to the negligible ventricular absorption was the high subarachnoid absorption in all except the two postmeningitic cases (Cases 5 and 6). The appearance time in the urine and the duration of excretion following subarachnoid injections were normal.

This type of internal hydrocephalus results because the cerebrospinal fluid cannot escape from its place of origin in the ventricles,

where the absorption is negligible, to the subarachnoid space, where the absorption normally occurs, because the channels of communication are occluded (Fig. 21).

GROUP 2.—INTERNAL HYDROCEPHALUS WITH FREE COMMUNICATION BETWEEN THE VENTRICLES AND THE SUBARACHNOID SPACE

CASE 8.—R. G., aged 1½ years. Diagnosis: Internal hydrocephalus.

Clinical Note.—Family History: Three other children living and well. No history of syphilis or hydrocephalus.

Past History: Full term. Weight at birth, 12 pounds. Spontaneous delivery. Patient held up head at the fourth month, sat up at the sixth month. Dentition began at the seventh month. He appeared a normal baby in every respect until 7 months of age.

Present Illness: When 7 months of age, he became ill with high fever, vomiting, great irritability and muscular rigidity. This condition lasted for three days and during the following two weeks he had an irregular fever. The appetite was poor and he lost in weight. After this illness the patient was unable to hold up his head. One month later it was noticed that the head was larger than normal and that the eyes were pushed downward. For the next three months, the head continued to increase rapidly in size.

Examination: The patient was a well-developed and well-nourished infant. The head measured 52 cm. in circumference. He was unable to raise his head. The child saw and heard and recognized the members of his family. The forehead was prominent and the occiput flattened. The anterior fontanel was widely open and the sutures separated. The eyes were displaced downward and there was weakness of both external recti. The eye-grounds were normal. The reflexes were active and equal; a bilateral ankle clonus was present.

Spinal Fluid: Clear, 6 cells per cubic millimeter. Noguchi globulin test, negative.

Ventricular Fluid: Clear, 6 cells per cubic millimeter. Noguchi globulin test, negative.

Tests.—1. There was communication between the ventricles and the subarachnoid space. Phenolsulphonephthalein was demonstrated in the spinal fluid *two minutes* after ventricular introduction. The test was repeated after one month and phenolsulphonephthalein appeared in the spinal fluid in one minute. 2. After ventricular introduction phenolsulphonephthalein appeared in the urine in thirty minutes and *2 per cent. was excreted in two hours*. One month later, the test was repeated and phenolsulphonephthalein appeared in the urine in twenty minutes and *2.3 per cent. was excreted in two hours*. 3. After subarachnoid introduction, *11 per cent. of phenolsulphonephthalein was excreted in two hours*. At the second test, phenolsulphonephthalein appeared in the urine in thirteen minutes and *7 per cent. was excreted in two hours*.

Remarks.—From the history it seemed very definite that an attack of meningitis was the etiological factor responsible for the development of the internal hydrocephalus. From the rapid passage of fluid from the ventricles to the subarachnoid space it was evident that free communication existed. The absorption from the subarachnoid space was much diminished, from 7 to 11 per cent. of phenolsulphonephthalein, as opposed to the normal of 35 per cent. or over. The appearance of the dye in the urine following its introduction into the ventricles and into the subarachnoid space was also much delayed. The kidney function test was normal.

CASE 9.—M. R., aged 11 months. Diagnosis: Cerebrospinal meningitis with secondary internal hydrocephalus.

Clinical Note.—Family History: No history of syphilis or hydrocephalus.

Past History: Only child, full term, normal delivery; breast fed. Dentition began at fourth month. Sat up at eight months. Always well until present illness.

Present Illness: This began suddenly three days before admission to the outpatient department (March 31, 1913) with high fever, drowsiness, vomiting and extreme irritability. She had had one convulsion. Temperature 101.6 F.

The following note was made: "An irritable colored girl, aged 11 months, appears very sick. She is well-nourished and well-developed. There is slight cervical rigidity. The sudden onset, drowsiness, fever, vomiting, convulsion and rigidity of the neck suggest meningitis." Lumbar puncture was not allowed and hospital treatment was refused by the parents. The first two weeks after the onset the baby was very sick. About April 12 she was unconscious for five days. Two weeks later (April 26, 1913) she vomited and began to have twitching movements of the face and extremities.

On admission to the hospital (May 2, 1913) the child, greatly emaciated, was in a stupor from which it was difficult to arouse her. The head measured 45 cm. in circumference, the anterior fontanel was small. The pupils reacted slowly to light. Vision was evidently impaired. There was rigidity of the extremities, exaggerated reflexes and ankle clonus. Temperature, 102 F. Leukocytes, 14,400. Von Pirquet test, negative.

Spinal Fluid: Twenty c.c. turbid fluid. Noguchi globulin reaction, positive; culture showed no growth. Smear: Many pus cells, no organisms.

Thirteen c.c. of antimeningitic serum were injected. The patient was removed from the hospital by her parents after twenty-four hours. The child was brought to the dispensary seven weeks later (June 25, 1913) because she could not see. On examination in the ward, July 5, 1913, the patient was poorly nourished, apparently blind, and very sensitive to sounds. The head was retracted and the neck rigid and there was spasticity of the extremities. The head measured 45 cm. in circumference. The pupils were unequal and reacted only slightly to light. There was no choking of the disks. There was a vertical and lateral nystagmus. Kernig's sign was positive. The reflexes were exaggerated and a bilateral ankle clonus was present. Temperature, 98.6 F. Leukocytes, 12,000. Wassermann reaction, negative.

Spinal Fluid: Clear, 10 c.c. Forty-two cells per cubic millimeter; Noguchi globulin reaction, positive; cultures negative; tubercle bacilli not found.

Ventricular Fluid: Clear fluid, 12 cells per cubic millimeter; Noguchi globulin reaction, positive.

The child was taken home after a few days, having made no improvement.

Tests.—1. There was communication between the ventricles and the subarachnoid spaces. Phenolsulphonaphthalein appeared in the spinal subarachnoid space *seven minutes* after being introduced into the ventricle. 2. After ventricular introduction, phenolsulphonaphthalein appeared in the urine in thirteen minutes and *6.5 per cent. was excreted in two hours*. Later (two and one-half months) a second test was made and phenolsulphonaphthalein appeared in the urine in twenty minutes and only *0.5 per cent. was excreted*. 3. After subarachnoid introduction, phenolsulphonaphthalein appeared in the urine in eight minutes and *14 per cent. was excreted in two hours*. Two days later this test was repeated and 9.5 per cent. of phenolsulphonaphthalein was excreted in two hours. It was being excreted in the urine after seventy-two hours. 4. The kidney function was normal.

Remarks.—The child was seen at the onset of an attack of epidemic cerebrospinal meningitis. A month afterward she was brought to the hospital because of beginning blindness. The absorption after ventricular injection was low (about 50 per cent. of the normal). The patient was admitted to the hospital two months after the onset, totally blind, and hydrocephalus was evident. There was very marked diminution in absorption, only 0.5 per cent. after ventricular injection and 9.5 per cent. and 15 per cent. from the subarachnoid

space. Free communication existed between the ventricles and the subarachnoid space.

CASE 10.—H. N., aged 8 months. Diagnosis: Internal hydrocephalus.⁴

Clinical Note.—Family History: No other cases of hydrocephalus in the family.

Examination: The child was well-nourished. The head measured 51 cm. in circumference. The anterior fontanel measured 10 by 8 cm.; it was tense and slightly bulging. There was a bilateral choked disk. The knee-reflexes were exaggerated though equal. Two and one-half weeks after the first admission the patient's head had increased 2 cm. in size. During another interval of eighteen days the head increased 0.9 cm. in circumference. At this time lumbar puncture was repeatedly done and fluid withdrawn for its therapeutic effect. Following this mode of treatment the child became able to hold up its head and the increase in size became less rapid. The Wassermann test was negative for the blood and the ventricular and spinal fluids. Von Pirquet test, negative.

Ventricular Fluid: Clear, 6 cells per cubic millimeter. Noguchi globulin test, negative.

Spinal Fluid: Clear, 6 cells per cubic millimeter. Noguchi globulin test negative.

Tests.—1. Communication was demonstrated between the ventricles and the subarachnoid space. Phenolsulphonephthalein appeared in the spinal fluid *twenty minutes* after its introduction into the ventricle. 2. Phenolsulphonephthalein appeared in the urine *twenty-five minutes* after its introduction into the ventricles and *4.4 per cent. was excreted in two hours*. Two weeks later, the absorption was 4 per cent. 3. The absorption from the subarachnoid space was *10 per cent. during a two-hour period*. The same result was obtained two weeks later. 4. The kidney function test was normal.

Remarks.—Except for the brief illness shortly after birth there was nothing to suggest a cause for the hydrocephalus. We were unable to obtain any information either from the mother or the attending physician to warrant a diagnosis of meningitis. The clinical tests showed that there was a delayed absorption from the subarachnoid space. The time of appearance in the spinal canal following the ventricular injection was much longer than in either of the two preceding cases of this group. That there was adequate communication, however, was shown by the relatively high concentration of phenolsulphonephthalein in the spinal fluid two and one-half hours after the ventricular injection.

CASE 11.—J. C., aged 16 months. Diagnosis: Internal hydrocephalus.

Clinical Note.—Only child. Parents, healthy; instrumental and prolonged labor (thirty-one hours). A cephalhematoma developed soon after birth and disappeared in five weeks. The primary respirations were difficult to establish. No convulsions. The enlargement of head was not noticed at birth. The head appeared large when he was 3 months of age and thereafter steadily increased in size. In six weeks it increased 2 inches, and in two weeks $\frac{3}{4}$ inch. January, 1913, the head measured 55.5 cm.; September, 69.5 cm., and November, 1913, 72.5 cm. The child never had fever or convulsions or any illness suggesting meningitis.

Examination: The head was large and measured 72 cm. in circumference. The reflexes were exaggerated. The Wassermann reaction of the spinal fluid and blood was negative.

7. The phenolsulphonephthalein tests in this case demonstrated a communicating type of hydrocephalus. Repeated lumbar punctures were made for their therapeutic effect. The process has remained stationary for three months and the child is apparently cured.

By lumbar puncture from 40 to 75 c.c. of clear fluid were obtained. Six cells per cubic millimeter. Globulin test, negative. Fehling's, slight reduction.

Tests.—1. There was communication between the ventricles and subarachnoid space. Phenolsulphonephthalein appeared in the spinal fluid in less than one minute after its introduction in the ventricle. 2. The absorption following the introduction of phenolsulphonephthalein in the ventricles was 4 per cent. in two hours and the time of appearance in the urine was forty minutes.

Remarks. A subarachnoid test was not obtained. It was evident, however, from the rapid appearance of phenolsulphonephthalein in the subarachnoid space that communication was adequate.

SUMMARY OF CASES IN GROUP 2

In this type of hydrocephalus the communication between the ventricles and the subarachnoid space is patent, thus differing from Type 1, in which there is no communication between the ventricles and the

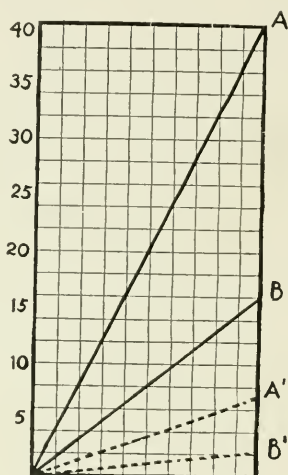


Fig. 22.—Curve comparing the normal ventricular and subarachnoid absorption with the absorption in internal hydrocephalus of the communicating type. The base line represents a two-hour period and the vertical line represents the absorption (percentage of phenolsulphonephthalein excreted) during this time. The heavy lines represent the normal absorption and the dotted lines the absorption in hydrocephalus. A, normal subarachnoid absorption; A', absorption from subarachnoid space in communicating hydrocephalus; B, normal absorption of fluid placed in the ventricles; B', absorption of fluid placed in ventricles of communicating hydrocephalus.

subarachnoid space. Following intraventricular introduction of phenolsulphonephthalein, the dye appears almost immediately (from one to seven minutes) in the spinal fluid. In one case of this group on two separate occasions the time of appearance in the spinal fluid was delayed to fifteen and twenty minutes. We were unable to determine the reason for this delay. Communication in this type of hydrocephalus is further proved by the rapid appearance in the ventricular fluid of

phenolsulphonephthalein after being introduced into the subarachnoid space.

The absorption from the subarachnoid space of these patients is greatly diminished (about 10 per cent. in two hours). There is a corresponding increase in the time of first appearance of phenolsulphonephthalein in the urine and in the time required for its total excretion from the subarachnoid space. *The diminished subarachnoid absorption is the factor responsible for the production of the internal hydrocephalus (Fig. 22).*

The absorption after ventricular injection was also very low (about 4 per cent.), but distinctly higher than in Group 1. *Since it has been shown that there is practically no absorption from the ventricles, the absorption following ventricular injection in normal cases or in cases of internal hydrocephalus of the communicating type must be due to absorption from the subarachnoid space after the fluid has passed through the foramina of exit from the ventricles.*

We have had no pathological examination on patients with hydrocephalus of this type demonstrated by these clinical tests. It is very likely that the diminished absorption from the subarachnoid space is due to adhesions which diminish the size of the subarachnoid space. Adhesions anterior to the foramina of Luschka, by causing obliteration of the cisterna magna, would prevent the passage of fluid into the general cerebral subarachnoid space as effectually as if the aqueduct of Sylvius were obliterated. The two groups would then be essentially similar, differing only in the fact that the spinal subarachnoid space participated in absorption in the communicating type. When there are adhesions at the base of the brain they are frequently present also between the cord and the meninges.

We have had the opportunity of examining the specimen from a patient who had hydrocephalus of this variety. There was a congenital internal hydrocephalus evidently the result of an intra-uterine meningitis. Dense adhesions were found along the cord and the base of the brain obliterating the cisterna magna. The foramen of Magendie was sealed by adhesions, but the foramina of Luschka were patent and greatly dilated. There was no cisterna for the reception of fluid.

How much alteration in the meninges alone, without adhesions, interferes with absorption, cannot be stated. It seems to us probable that the major part if not all of the disturbance is due to the limitation of the subarachnoid space.

That there is another type of hydrocephalus intermediate between Group 1 and Group 2 appears probable. There must be cases in which the obstruction to the outflow of fluid from the ventricles is not complete but partial, and in which the subarachnoid absorption is either

normal or diminished. With such a combination a hydrocephalus must also result. Indeed, Case 6 (Group 1, F. W.) probably belongs to this intermediate group. That there was a slight communication was shown by the trace of phenolsulphonephthalein in the spinal fluid after ventricular introduction. The subarachnoid absorption was greatly diminished and corresponded in amount with the absorption found in the cases of Group 2. The slightly higher absorption, 2 per cent. after ventricular introduction, is probably also to be explained by a partial communication. At a later observation a complete obstruction was found and the ventricular absorption was much less.

10. *CLINICAL DIFFERENCES BETWEEN THE COMMUNICATING AND OBSTRUCTIVE TYPES OF INTERNAL HYDROCEPHALUS*

There is no way by which a differentiation can be made between the obstructive and the communicating types of internal hydrocephalus except by the actual determination of the presence or the absence of communication between the ventricles and the subarachnoid space. While the increase in size of the head appears usually to be slower in many cases in which there is communication, there are other cases in which the increase is very rapid.

It is sometimes possible to tell by the large amount of fluid removed by lumbar puncture that the case is of the communicating type. This can be, however, only when the internal hydrocephalus is advanced in degree. When there is obstruction either at the aqueduct of Sylvius or at the foramina of Luschka and Magendie, 25 c.c. or more of fluid can frequently be obtained by lumbar puncture and the erroneous conclusion might be reached that the fluid was withdrawn from the ventricles. Differences in the cell count and in serological tests, between the spinal and ventricular fluids, are usually too slight to be of any value.

The only satisfactory method of differentiating these two groups is by the phenolsulphonephthalein test as described above.

11. *THE RELATION OF OBSTRUCTION TO INTERNAL HYDROCEPHALUS*

That obstruction may be responsible for internal hydrocephalus was first demonstrated by Magendie. John Hilton accepted Magendie's views and thought that probably every case was so produced. In his excellent lectures on "Rest and Pain," drawings are given to show the obstruction which he found quite constantly. Quinke, Bourneville and Noir, Spiller, Browning, Schlapp and Géré, Neurath and numerous other writers reported cases showing various types of occlusion which were held responsible for the internal hydrocephalus. Obstruc-

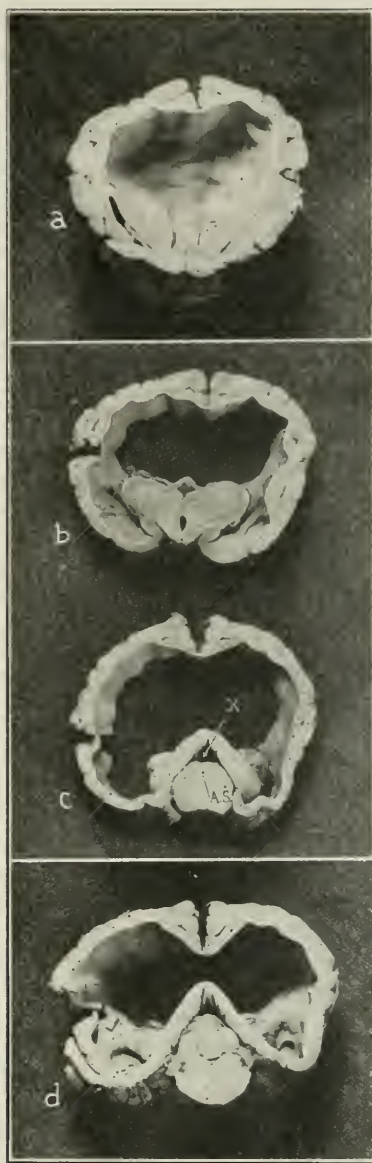


Fig. 23.—Spontaneous internal hydrocephalus in a dog found by Dr. A. P. Jones. The aqueduct of Sylvius (*A. S.*) is completely occluded. The lateral ventricles form a single cavity owing to the absorption of the septum lucidum. A free communication is present between the third ventricle and the subdural space at *X*, but the hydrocephalus is not modified owing to the poor absorption from the subdural space. Note the small fourth ventricle posterior to the obstruction.

tions have been observed at the foramina of Monro producing a unilateral hydrocephalus, at the aqueduct of Sylvius producing dilatation of the third and lateral ventricles, and at the foramina of Luschka and Magendie producing enlargement of all the ventricles. The obstructions have been due to inflammations, tumors and congenital defects. Obstructions have also been noted in animals, especially in the horse, cow, dog and cat (Fig. 23). Dexler studied many cases of hydrocephalus, known as *Dummkoller*, in the horse, and found quite constantly an occlusion of the foramina of Luschka. It will be recalled that the foramen of Magendie does not exist in the horse.

In our series of seven patients in whom an obstruction was determined by the phenolsulphonaphthalein test, necropsies were obtained in five, and in each of these the presence of an obstruction was demonstrated. Moreover, an obstruction experimentally placed in the aqueduct of Sylvius causes an internal hydrocephalus. Internal hydrocephalus is produced because the fluid forms in the ventricles and cannot escape to the subarachnoid space where it is absorbed. In this respect there is a close analogy between the ventricles of the brain and the renal pelvis. Just as hydronephrosis results from obstruction along the course of the ureter, so a hydrocephalus results from an occlusion of the channels of exit from the ventricles. In neither the pelvis of the kidney nor the ventricles of the brain is there sufficient absorption to overcome the effects of occlusion.

12. THE RELATION OF MENINGITIS TO INTERNAL HYDROCEPHALUS

In two specimens (Group 1) it was shown after the pathological examination that adhesions occluding the communicating foramina were responsible for the hydrocephalus. These were undoubtedly the result of a previous meningitis. In Group 2, two patients gave a definite history of meningitis, immediately preceding the onset of the internal hydrocephalus. Case 9 (M. R.) of Group 2 was seen during an attack of epidemic meningitis and during the subsequent development of the hydrocephalus. Case 8 (R. G.), Group 2, gave a typical history of meningitis. Before this illness the child was perfectly well and afterward he was not able to hold up his head and his head had enlarged.

Case 6 of Group 1 was an example of congenital hydrocephalus with a meningocele. Post-mortem examination, however, revealed the evidences of a marked basilar meningitis with occlusion of the foramina of Luschka and Magendie. There is, therefore, clinical and pathological evidence that meningitis is frequently the etiological factor in the production of internal hydrocephalus of both the obstructive and the communicating types, and there is every reason to believe that it occurs both before and after birth.

That meningitis is an important factor in the production of this disease has been clinically recognized at least since the beginning of the nineteenth century. Alexander Monro (1827) observed that hydrocephalus apparently of postnatal origin was frequently preceded by a severe illness, which was not then recognized as meningitis. Greater attention was directed to this disease as an etiological factor by Trousseau (1857), Foerster (1863), Ziemsen and Hess (1874). Joslin, Koplik, Gildesheim, Barlow and Lees, and Göppert recently called attention to the importance of this disease as a cause of internal hydrocephalus.

The pathological changes reported by various observers have not been uniform. Barlow and Lees, Hildesheim, and Bettencourt and Franca believe that the process always occluded the foramina of Magendie and Luschka. Barlow and Lees observed only two cases in a large series in which no occlusion was found and thought the hydrocephalus in these cases was due to an overproduction of fluid. Göppert, from post-mortem examination of twenty-three cases, classified the anatomical findings under three types: (1) total occlusion, four cases; (2) foramen of Magendie closed, but the foramina of Luschka large, six cases; (3) all the foramina patent, thirteen cases. Göppert's determination of the patency or occlusion of these openings was made by granular injections into the ventricles post mortem. The results of most observers have been based on inspection of the base of the brain, from which it is impossible to determine the condition of the foramina with certainty.

Why an internal hydrocephalus should result with patent foramina has never been demonstrated. We are unable to give the pathological basis for hydrocephalus of the communicating type owing to the fact that all of our patients are living; but the evidence here presented gives an explanation for the production of this type of hydrocephalus.

13. THE RELATION OF VENOUS STASIS TO INTERNAL HYDROCEPHALUS

Venous stasis due to obstruction of the small or the large veins of Galen is undoubtedly the cause of a small percentage of the cases of internal hydrocephalus. Experimental proof of this has been given. Internal hydrocephalus resulting from thrombosis by these veins has also been reported. Although such a cause of hydrocephalus is infrequent, it should always be looked for post mortem. It is also possible that tumors in the region of the midbrain might exert sufficient pressure to obstruct either the aqueduct or the veins of Galen. We are inclined to regard venous stasis as being of relative minor importance in the production of hydrocephalus.

Certainly in very young children tumors are uncommon, and the obstructive process is usually insufficient to produce a simultaneous involvement of the veins. In adults, among whom tumors are more common, it may play a more frequent but always a subsidiary rôle, because the aqueduct of Sylvius will usually also be occluded.

14. THE POSSIBILITY OF OTHER CAUSES OF INTERNAL HYDROCEPHALUS

Almost every conceivable cause, direct and indirect, has been suggested as being responsible for hydrocephalus. Alcohol, rickets, trauma, tuberculosis, syphilis, heredity, psychic disturbance during

TABLE 6.—SUMMARY OF GROUP 2, INTERNAL—

Case	Illness	Absorption after Ventricular Introduction		Absorption after Spinal Introduction		Communication between Ventricular and Subarachnoid space
		Time of appearance Minutes	Two-hour absorption Per cent.	Time of appearance Minutes	Two-hour absorption Per cent.	Time of Appearance in Spinal Canal following Ventricular Introduction—Minutes
8. R. G.	Internal hydrocephalus	30	2.	Not obt.	11	1
9. M. R.	Internal hydrocephalus following epidemic meningitis	20	2.3	13	7	2
		13-15	6.5	7 —
10. H. N.	Two months later	20	0.5	8	14	2
	Internal hydrocephalus	25	4.4	Not obt.	9.5 10	20
11. J. C.	Internal hydrocephalus	About 25	4	Not obt.	10	13
		30	4	0	0	1

* No post-mortem examination in any case.

pregnancy, lack of resistance of the brain tissue, osteogenetic defects of the skull and many other less likely possibilities have been suggested. Syphilis is undoubtedly responsible for a certain number of cases, but to cause hydrocephalus, syphilis must produce a lesion which involves the cerebrospinal spaces and cause a diminished absorption of cerebrospinal fluid either by occlusion of the foramina or by an affection of the meninges. In not one of our cases was there any evidence by serological test that syphilis was the etiological factor. Elsner thought syphilis responsible in three cases out of eighteen, and Hedenfeld in

10 per cent. of his cases. It is very unlikely that as systemic diseases without localized manifestations syphilis, tuberculosis, rickets and alcoholism have any etiological bearing on the production of internal hydrocephalus.

There was no familial or hereditary history of hydrocephalus in our cases. Göhlis reports an instance of a woman who gave birth to six still-born, hydrocephalic children.

The production of hydrocephalus by trauma is very difficult to prove. We have seen one case (not here recorded) in which the father, who was a physician, insisted that the onset of the disease dated

—HYDROCEPHALUS WITHOUT OBSTRUCTION *

Duration of excretion after		Kidney function 2 hours Per cent.	Etiology
Ventricular introduction	Spinal introduction		
Longer than 2 days	0	44	Definite history of meningitis. Hydrocephalus followed immediately. Followed meningitis.
.....	More than 24 hrs.	40 (1st hr.)	
.....	45	Hydrocephalus noted 6 weeks after birth. May have resulted from illness 3 days after birth.
.....		
0	0	Not tested.	

from a severe fall. Various congenital anomalies have been associated with hydrocephalus, such as hydrothorax, absence of kidney, cleft palate, bicornuate uterus, etc. The occurrence of internal hydrocephalus with spina bifida has been frequently noted. There were three such instances present in our series of cases.

Lack of resistance of cerebral tissue and imperfect development of the skull, though frequently suggested as causes of hydrocephalus, have been mentioned merely as possibilities. The cerebral atrophy and non-union of the sutures of the skull are undoubtedly secondary manifestations of the intracranial pressure.

15. INTERNAL HYDROCEPHALUS FOLLOWING THE REMOVAL OF A MENINGOCELE

Internal hydrocephalus following the extirpation of a meningocele has been frequently reported, but the cause for its development has never been satisfactorily explained. Muscatello, who has reported a series of cases of this character, attributed the hydrocephalus to an operative infection. His reason for doing this was based on the frequency with which ulceration of the meningocele was observed.

From our observations on the general character of absorption of fluid from the subarachnoid space, it is most likely that the hydrocephalus results from a diminution in the absorption of the cerebrospinal fluid. This diminished absorption takes place because a large part of the absorbing surface is removed at the time of the operation.

Before removing a meningocele, it is important to determine the absorption from the subarachnoid space in order to determine whether or not it is sufficient. If absorption is below the normal, operation in the light of our present knowledge would be contra-indicated.

16. SUGGESTIONS AS TO THE TREATMENT OF INTERNAL HYDROCEPHALUS

We have shown that there are two types of internal hydrocephalus differing physiologically and anatomically, and it is obvious that an entirely different therapy is necessary for each variety. In the treatment it is important to know which type of hydrocephalus is present — the obstructive or the communicating. This can be determined by the phenolsulphonephthalein test.

In the obstructive type of internal hydrocephalus, the treatment should be directed toward removal of the obstruction. If this is at the foramina of Magendie and Luschka, as in Cases 5 and 6 of Group 1, the obstruction without doubt could be relieved. If the occlusion is located at the aqueduct of Sylvius, as in Cases 2 and 3 of Group 1, the problem of making an opening is obviously more difficult, perhaps impossible. It would also be necessary, before undertaking such an operation, to determine the amount of absorption from the subarachnoid space. If there is a low subarachnoid absorption as in Case 6 of Group 1, it is probable that the relief of the obstruction would merely transform an internal hydrocephalus of the obstructive type into one of the communicating type.

In the communicating type, the internal hydrocephalus is the result of diminished absorption from the subarachnoid space. In one case the post-mortem findings indicated that adhesions from an old inflammation produced obliteration of the cisterna magna and prevented the

cerebral subarachnoid space from participation in the absorption. At present, the rational treatment in this type of hydrocephalus would be to drain the fluid into other tissues where there is adequate absorption.

17. SUMMARY AND CONCLUSIONS

An internal hydrocephalus was experimentally produced in dogs by placing an obstruction in the aqueduct of Sylvius.

It is therefore evident that the cerebrospinal fluid is formed in the ventricles faster than it can be absorbed, and that the aqueduct of Sylvius is essential for its escape.

An internal hydrocephalus resulted from placing an obstruction in the aqueduct of Sylvius in spite of the extirpation of the choroid plexus of both lateral ventricles. This procedure apparently modifies the grade of the internal hydrocephalus.

An internal hydrocephalus may also result from an experimental ligation of the vena Galena magna near its origin; when the ligature is more distally placed or when the sinus rectus alone is ligated, an internal hydrocephalus does not result, owing to the efficient venous collateral circulation.

Cerebrospinal fluid is derived mainly from the choroid plexuses, probably both by filtration and by secretion.

An increase of cerebrospinal fluid is caused by general venous congestion as demonstrated by temporary jugular compression. This increase of fluid ceases when the congestion is relieved by the collateral circulation.

Drugs and glandular extracts produce but slight change in the rapidity of formation of cerebrospinal fluid. Pilocarpin produced a slight increase.

There is a definite impermeability of the fluid-forming structures. Of the various substances in solution in the blood, only traces of a few find their way into the cerebrospinal fluid. The cerebrospinal fluid is more strongly protected from substances in the blood than the peritoneal, pleural and pericardial fluids.

There is a rapid and constant formation and absorption of cerebrospinal fluid. A new supply is formed and absorbed at least every four to six hours.

The lymphatics play a negligible part in the absorption of cerebrospinal fluid.

Cerebrospinal fluid is absorbed directly into the blood. Absorption is from the entire subarachnoid space. It is a diffuse process and does not take place through specialized structures such as the pacchionian granulations or through stomata opening into the venous sinuses. That

stomata do not exist is demonstrated by the fact that granules do not readily pass from the subarachnoid space into the blood.

There is practically no absorption from the ventricles.

The maintenance of an equilibrium between the formation and the absorption of cerebrospinal fluid necessitates a communication between the ventricles and the subarachnoid space.

Communication is solely by the foramina of Magendie and Luschka.

After the introduction of phenolsulphonephthalein into the subarachnoid space it soon appears in the lateral ventricles. There are therefore no valves at these openings.

If an obstruction exists at the aqueduct of Sylvius, phenolsulphonephthalein does not appear in the spinal fluid. The so-called foramina of Mierzejewsky and Bichat therefore do not exist.

Granules placed in the subarachnoid space, without pressure, are soon uniformly distributed throughout the entire spinal and cerebral subarachnoid space. There is no evidence of a current to the region of the venous sinuses. Granules pass along the olfactory and optic nerves, over the gasserian ganglion of the trigeminal nerve and a short distance along the auditory nerves, but not along the remaining cranial and spinal nerves.

Internal hydrocephalus can be divided into two anatomically different types, depending on the patency or occlusion of communication between the ventricles and the subarachnoid space.

In seven patients with internal hydrocephalus lack of communication was demonstrated clinically. In each of these seven cases there was practically no absorption from the ventricles, while the subarachnoid absorption was high. The internal hydrocephalus, therefore, resulted because the passage of fluid from the ventricles into the subarachnoid space was prevented.

Four cases of internal hydrocephalus in which there was communication between the ventricles and the subarachnoid space were studied. In these cases there was a low subarachnoid absorption. Meningitis was the cause of the hydrocephalus in two patients with the obstructive type and two with the communicating type of hydrocephalus.

The probable cause of internal hydrocephalus following the excision of a meningocele is the limitation of absorbing surface and consequent diminution in the absorption of cerebrospinal fluid.

Surgical treatment differs according to the variety of internal hydrocephalus. *In the obstructive type* the obstruction must be removed. *In the communicating type* it is necessary to increase the area for the absorption of fluid.

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